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SULFATHIAZOLE THERAPY OF FIVE HUNDRED PROSTITUTES WITH CHRONIC GONORRHEA

THE CONTROL OF VENEREAL DISEASE IN WARTIME

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Medical history shows that there is a great increase of venereal disease during wartime. Prostitutes are a danger to our military and industrial army. Detailed histories of some of our cases reveal twenty to thirty exposures during a twenty-four hour period. In a metropolitan city like New York with huge naval, military and industrial developments, a center for the armed forces on leave or embarkation, this problem assumes such serious significance that it requires immediate and proper attention.

This paper is based on a study of 615 women, culturally positive for the gonococcus, who were hospitalized at the Kingston Avenue Hospital. They had been arrested for actual or attempted prostitution, tried at the Jefferson Market Court and found not guilty or given suspended sentences. However, since they had gonorrhea, the Health Department immediately ordered them hospitalized for treatment as a means of controlling the spread of venereal disease.

Only 20 per cent of these patients, all culturally positive, were noted to have clinical evidence of gonorrhea at the time of the initial examination at our hospital. Repeated examinations revealed a greatly increased percentage of clinically positive cases, owing partly to the discovery and discounting of deceptive methods employed by the patients and partly to the greater accuracy resulting from repeated checkups.

On admission a complete history, including the gynecologic and sociological aspects, was taken, and a general physical examination was done. Then a thorough gynecologic examination, which included the urethra, Skene's and Bartholin's glands, the cervix, corpus and adnexa, was made by both the resident and the visiting staff. Spreads and cultures were taken from the urethra, cervix and, when indicated, from Skene's and Bartholin's glands. Blood for the Wassermann test and the complement fixation test for gonorrhea as well as complete blood counts and urinalyses were performed routinely. When indicated, additional cultures and spreads, sedimentation rates, blood chemical examinations and sulfathiazole determinations were done.

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The routine treatment was the administration of sulfathiazole orally in four doses between 6 a. m. and 10 p. m. The patients were ordered to take a minimum of 1,500 cc. of fluids daily and to report a diminished urinary output, hematuria or other toxic symptoms. They were advised to avoid direct sunlight. About 20 per cent of these girls received mapharsen concurrently for their syphilis. Urinalyses and blood counts were repeated routinely during the course of treatment. Dosage was not based on body weight.

These 488 patients were divided into three groups among which the duration of treatment and/or the daily dosage varied. Group 1 received 45 grains (3 Gm.) daily for ten days, group 2 received 60 grains (4 Gm.) daily for ten days and group 3 received 60 grains daily for seven days. Local therapy was not used in this series, nor was sulfanilamide. Sulfapyridine, because of its greater toxicity, was used only in some cases when sulfathiazole failed.

The first smear after completion of treatment was taken on the fifth day. At four day intervals thereafter both smears and cultures were taken. At least one smear and culture was taken during or immediately after menstruation. Careful speculum examinations emphasizing the amount, consistency and color of the discharge were made during and after chemotherapy by several members of the staff.

Specimens for culture consisted of swabs taken from the source of the discharge. These were placed in tubes containing 1 to 2 cc. of 2 per cent proteose peptone No. 3 solution in 0.5 per cent sodium chloride. They were thus transported to the laboratory, where they were inoculated in less than two hours after delivery.

The medium employed was the Difco product recommended by Carpenter. Difco proteose peptone No. 3 agar is prepared double strength. Equal quantities of this and a 2 per cent bacto-hemoglobin are mixed under aseptic conditions and plates poured. The swab was removed from the tube and streaked over two thirds of the plate and was rolled from side to side to insure inoculation of all the material. The plate was streaked with a platinum wire at right angles to the original streak to insure dilution and growth of discrete colonies. Approximately 12 per cent of the air was removed and replaced by carbon dioxide. The plates were incubated at 35 C. for forty-eight hours in air tight jars. At the end of this time the plates were read first by direct inspection and then with a 1 per cent solution of dimethylparaphenylenediamine monohydrochloride poured over suspected colonies by medicine dropper. If a smear from an oxydase positive colony showed typical gram negative biscuit shaped diplococci and a subculture from such a colony failed to grow on nutrient agar at room temperature, such a culture was considered to be a gonococcus. However, if repeated cultures continued to be positive, further subcultures were made to chocolate agar, plain agar and sugar fermentation mediums (dextrose, maltose and saccharose).

The cultures taken in this laboratory are repeat cultures. The primary cultures were taken by the New York City Health Department.

The minimum requirements for discharge from Kingston Avenue Hospital were four consecutive negative smears and three cultures. In addition it was required that there should be no gross clinical evidence of the disease. (Even all of the foregoing prerequisites in our opinion do not constitute adequate proof of cure because of the relatively brief period of observation.)

When the dosage was raised from 45 grains daily (group 1, total 30 Gm.) to 60 grains daily (group 2, total 40 Gm.) for ten days the percentage of apparent

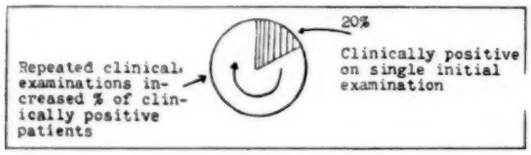
20%
Clinically positive on single initial examination
Repeated clinical examinations increased % of clinically positive patients

Chart 1.—Culturally positive 100 per cent.

cures was raised by 8.1 and there was no appreciable increase in toxic symptoms. Then the period of treatment was decreased from ten days to seven days with the daily dosage remaining at 60 grains (group 3). The total dosage dropped from 40 Gm. to 28 Gm. The 2.7 per cent increased cure rate, however, has no statistical significance, in our opinion.

In only 2 cases in the entire series did toxic symptoms necessitate interruption of therapy. The first patient had a mild secondary anemia before taking sulfathiazole, i. e. 45 grains daily for ten days. Later, since she represented a failure, 60 grains of sulfapyridine was given for only three days because she developed a pronounced secondary anemia necessitating a blood transfusion. Without further therapy her cultures became negative and she was discharged. The second patient on the fourth day, after taking 240 grains (15 Gm.) developed hyperpyrexia, reddened throat, stiff neck, pain and tenderness in the lower part of the abdomen and in the renal areas. She recovered promptly on stopping the sulfathiazole. Symptoms recurred after a repetition of only 60 grains of the drug.

Minor toxic symptoms (i. e. headache, dizziness, slight nausea, faint and transient rashes) were occasionally encountered. However, in none of these cases was it necessary to discontinue treatment.

The vast majority of the patients felt well, had no complaints and usually gained weight. The average net gain in body weight was 2.83 pounds (the maxi-

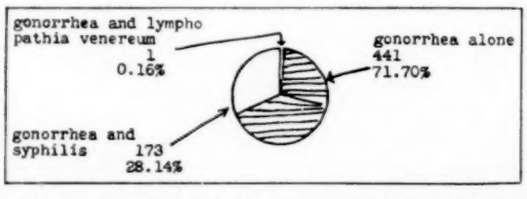

Chart 2.—Six hundred and fifteen patients with positive gonococcus culture: 441 (71.70 per cent) had gonorrhea alone, 173 (28.14 per cent) had gonorrhea and syphilis, and 1 (0.16 per cent) had gonorrhea and lymphopathia venereum.

mum being 21 pounds and the minimum ¼ pound). The average period of hospitalization for those with gonorrhea alone was thirty-one days and for those with gonorrhea and syphilis was forty-five days. Most of the patients were between 20 and 30 years of age (the youngest 16 years and the oldest 49 years).

Of the 488 patients having completed treatment and discharged after four consecutive negative smears and three negative cultures, 441 (90.4 per cent) were negative after the first course of sulfathiazole and 47 (9.6 per cent) were failures after the first course. Of the 47 failures (after the first course) 42 became negative after the second course. [The second course was sulfathiazole in 39 cases. The second course was sulfapyridine in 8 cases, 7 of which were rendered negative immediately. The eighth one required focal therapy in addition and a third course of a sulfonamide compound (sulfathiazole)].

By giving a second course of sulfonamide compounds to the failures on the first course, the number rendered bacteriologically negative was raised from 441 to 483 and the percentage increased from 90.4 to 98.9. Five of the 47 were not bacteriologically negative after the second course. Of the 5 failures after the second course, 3 became negative after the third course of sulfonamides (the first and second courses were sulfathiazole, and the third was sulfapyridine). One became negative after cervical cauterization, having failed to respond to two previous courses of sulfathiazole. One failed after a third course (the first course was sulfathiazole, the second sulfapyridine, the third, sulfathiazole) but became negative after cervical coagulation.

Bacteriologic analysis of the 47 failures after completion of the first course of sulfathiazole therapy revealed that on the first bacteriologic check-up only 17 cases were positive, on the second check-up 10 more

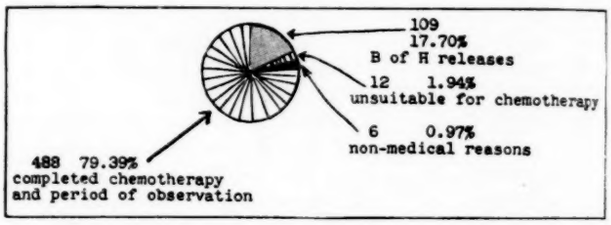

Chart 3.—Six hundred and fifteen patients with positive gonococcus culture.

cases were found positive, on the third check-up 18 additional cases were positive and on the fourth check-up 2 more cases were positive. The first check-up was made five days after completion of therapy and the subsequent ones at four day intervals.

It is obvious, therefore, that one or two negative bacteriologic observations are insufficient to determine cure. Negative evidence here as elsewhere has value only if it is corroborated by repeated identical findings. It follows that increasing the period of surveillance allowing for more check-ups diminishes the possibility of overlooking the asymptomatic carrier (latent cases).

The clinical picture may be distorted in some cases because of associated Trichomonas vaginalis vaginitis, which was present in 67 per cent of our cases on admission and which almost invariably persisted despite the sulfathiazole therapy.

In over 60 per cent of the cases a purulent cervical and urethral discharge, which was not caused by Trichomonas, persisted after completion of sulfathiazole treatment despite repeated negative cultures for the gonococcus. This persistent discharge was presumably due to sulfonamide resistant secondary invaders or to an inflammatory reaction caused by the preceding gonococcic infection. It seems advisable to apply in addition local treatment in order to eradicate this discharge.

If Skene's or Bartholin's glands were affected, discharge (though gonococcus negative) or swelling likewise persisted in many cases after sulfathiazole therapy.

Bartholin's gland abscess was present in approximately 1 per cent of our cases. The incidence of adnexal involvement and postmenstrual flare-ups has diminished definitely since sulfonamide medication has been instituted.

The persistence of a discharge which culturally appears nonspecific throws a heavy responsibility on the clinician when he is asked whether a patient is still infectious. If these patients were observed for a longer period of time, some of those with negative cultures might become positive again. All of us have observed on occasion a reversal of cultural findings after the first or second were negative. Perhaps this is because sulfathiazole is only bacteriostatic, and virulence may be subsequently restored because of failure of biologic response. This phenomenon seems to be partly substantiated by the observation that negative cultures have been found when the smears were simultaneously positive.

Since the immediate success or failure is not always related to the degree of sulfonamide concentration in

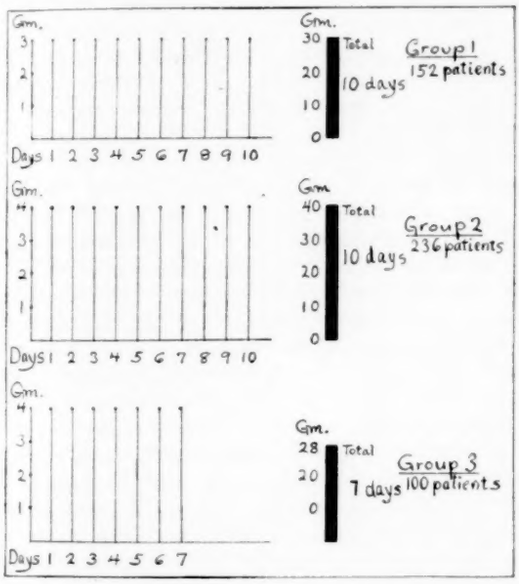

Chart 4.—Treatment of 488 patients with sulfathiazole.

the blood, we may assume that the fluctuations in cultural findings may be caused by immunologic changes producing increased resistance throughout the body or only in the affected mucous membranes or by a diminution in the viability of the gonococcus. Therefore the result of this therapy is either death of all the gonococci (i. e. definite cure) or only attenuation of the organism (i. e. an asymptomatic carrier). In either case the cultures may be found negative. In order to detect this asymptomatic carrier, who is a continuous source of infection, we must try to improve our diagnostic methods (cultural technic, culture mediums, provocatives and so on).

This resolves itself into the problem as to when these patients are no longer infectious. We must consider, first, clinical, bacteriologic and symptomatic cure for the patient's own sake; second, noninfectivity to others as a public health concern.

It has been well established that a known positive untreated case may yield negative cultures, and since we have no one test such as animal inoculation which definitely marks the time of clinical cure, we are left with but one alternative: we must use repeated cultures, smears and clinical observations over a sufficient period of time before passing final judgment. The almost incredible percentage of apparent cures should not cause us to relax our vigilance. We have found positive cultures, smears and/or clinical evidence after three negatives. We have also found little or no toxicity in this large series of patients who are otherwise healthy except for this usually local pathologic condition. Because of these two factors one should not hesitate to treat even doubtful cases.

TABLE 1.—*Patients Studied from July 1941 to June 1942 Inclusive*

Of these 615 patients:	
441 had gonorrhea alone	71.70%
173 had gonorrhea and syphilis	28.14%
1 had gonorrhea and lymphopathia venereum	0.16%
Of the 615 patients:	
109 were discharged by special release issued by the Director of the Bureau of Social Hygiene of the Department of Health before treatment was completed	
12 were considered as not suitable for chemotherapy and were excluded from this series	
6 did not complete treatment for nonmedical reasons:	
4 were sent to prison for arson	
1 escaped	
1 was transferred to another hospital	
127 therefore did not complete the treatment	
488 patients completed treatment and remained in the hospital an average of twenty-one additional days	

In our opinion at least four consecutive negative cultures and smears should be made at weekly intervals and the patient should be clinically negative and be under a further period of observation of at least six weeks before she can be reasonably regarded as noninfectious. Additional studies will prove whether it is safe to decrease the dosage, treatment time and the period of observation. The ultimate desideratum of cure in female gonorrhea will be the failure to reproduce the infection after human exposure.

With respect to the 109 infected patients discharged by the Department of Health by special releases before treatment was completed, the following is evident:

Assuming that only 100 of these 109 girls return to prostitution as a livelihood, and allowing them sixty-five days for idleness and menses, and granting the average number of daily exposures to be even less than their admitted minimum of twenty, approximately half a million men could be infected in a year while the girls are under private medical care and yet continue to practice their profession at the same time. The futility of follow-up in ambulant patients whose very livelihood depends on deliberate and persistent reexposure is obvious. When, in addition, the asymptomatic carrier is considered, the problem is complicated many fold.

TABLE 2.—*Treatment with Sulfathiazole*

Groups	Total Dosage, Gm.	Number of Patients	Negative on 3 Consecutive Cultures After a Single Course of Therapy	
			Number	Percentage
1.—45 grains daily for 10 days....	30	152	128	84.2
2.—60 grains daily for 10 days....	40	236	218	92.3 8.1%
3.—60 grains daily for 7 days.....	28	100	95	95.0 2.7%
Total.....		488	441	Average 90.5

It is clear, therefore, that prostitution by its very nature requires adequate hospitalization if there is to be not only proper treatment but also control of the spread of infection. Repeated offenders endangering the nation's health in wartime should be interned for the duration and educated to do useful work for the war effort. Above all, this may lead to their permanent rehabilitation. Equally obvious is the fact that the added cost of such hospitalization and rehabilitation will be more than offset by considerations of health and the undoubted prevention of loss of time and efficiency in our war industries and armed forces on whom our national safety depends.

SUMMARY AND CONCLUSIONS

A study of 615 hospitalized gonorrheal patients shows that 60 grains of sulfathiazole daily for one week gives a 95 per cent apparent cure rate. The administration of sulfathiazole or sulfapyridine to the failures increases this rate to 98.9 per cent.

This very high cure rate must, however, be carefully scrutinized in order to determine the permanence of our immediate results. It must be ascertained in each case whether there has been sufficient treatment and an adequate period of observation.

Furthermore, and most important, it must be determined whether the criteria of cure employed are sufficient to insure protection of the public against further infection. The difficulty in detecting the asymptomatic carrier cannot be emphasized too strongly. Health departments defeat their own purpose by hospitalizing patients to control infection and then releasing them before cure in the custody of a private physician, because of an interpretation based on the present law.

We feel that a prostitute, although treated, remains potentially infectious for approximately three months, during which time, if at large, she is a source of infection and as such forfeits her right to the benefit of doubt.

The cure of an infected prostitute requires adequate compulsory hospitalization. Repeated offenders should be interned for the duration and compelled to aid in the war effort. If the law now does not adequately remove this public health hazard, as it does in most contagion, remedial statutes should at once be enacted toward that end.

If the state can call on a man for his life in this grave emergency, surely the common welfare demands that the "right" of an infected prostitute to be at liberty while still infectious be disallowed, at least for the duration of the war.[1]

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1. Dr. E. A. Horowitz granted the use of those patients who were in his service. Dr. Julius Sass, pathologist, and Miss Lillian Robbins, bacteriologist, rendered assistance.

Choice of Words.—It is customary to describe one whose powers of expression are above the average as having a good 'choice of words.' This goes to the heart of the matter. Choice means careful selection and requires thought. The doctor who expresses himself with clarity and precision thinks before he speaks. He has established a lifelong habit which gives him speed in choosing the right word for any shade of meaning. Many have not acquired this habit and rely on the stereotyped solecisms of a strictly limited medical jargon, which comes so easily to the tongue. Too often these unworthy phrases find their way into print. No doubt the pendulum will swing again and the profession demand a higher standard of literary expression than at present prevails.—The Decay of Medical Language, editorial, *New Zealand M. J.* **41**:237 (Dec.) 1942.

TOXIC REACTIONS FOLLOWING THERAPY WITH SULFAPYRIDINE, SULFATHIAZOLE AND SULFADIAZINE

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The value of the sulfonamide drugs in the treatment of many infectious diseases is evidenced by their widespread use. As these drugs have been employed more frequently, physicians have become increasingly aware that certain toxic effects may follow their administration. A variety of toxic reactions have been described in the literature, all of which rightly serve to make physicians conscious of the hazards to be encountered when these compounds are given to patients. And yet, reports of individual instances or of groups of cases in which a complication occurred following the use of one of the sulfonamides will not serve to show the relative frequency of these complications or their severity and importance. These can best be portrayed from a study of a large group of patients treated and observed under uniform conditions. The present paper is an analysis of the toxic reactions encountered in all the patients treated with sulfapyridine, sulfathiazole or sulfadiazine whose treatment was personally observed by one or both of us up to Jan. 1, 1943 either at the Gallinger Municipal Hospital [1] or in private practice. Most of these patients were treated for pneumonia, but a great many were given sulfonamides for other infectious diseases, such as meningitis, endocarditis, gonococcic arthritis and pyelitis. A few of the patients were ambulatory. All patients had complete blood counts and urinalyses before the sulfonamides were started and frequently, usually every alternate day, thereafter as long as the drugs were being given. Determinations of the free blood sulfonamide level were done on hospital patients usually daily during the course of therapy. On a few of the patients, determinations of free and combined sulfonamides were made. Hospital patients were observed and questioned daily for the presence of toxic reactions, and ambulatory patients three times a week.

Table 1 shows the incidence of toxic reactions for each of the three sulfonamide drugs used. When two or more courses of a sulfonamide were given, only the first course is included in the table. It will be seen that the toxicity from sulfadiazine was less than that following sulfathiazole, which in turn was less than that obtained with the use of sulfapyridine. Among 498 patients treated with sulfapyridine, toxic reactions occurred in 149, or 29.9 per cent. Fifty-eight, or 11.8 per cent, of the 321 patients receiving sulfathiazole suffered from toxic effects, while among the 660 patients to whom sulfadiazine [2] was administered only 51, or 7.7 per cent, experienced toxic symptoms. These differences were found to be significant when tested by the chi square method. The greatest difference

Miss Ruth Mayer rendered technical assistance and Miss Louise Mause assisted in the tabulations.

Dr. Lewis K. Sweet cooperated in the treatment of the patients from the Infectious Disease Service who are included in this report.

From the George Washington Medical Division, Gallinger Municipal Hospital, and the Department of Medicine, George Washington University School of Medicine.

1. Several of our former colleagues have cooperated in this work at different times, including Drs. T. J. Abernethy, Harry A. Feldman, Clarence R. Hartman, Frank A. Jenkins and Samuel J. Sugar.

2. The sulfadiazine and sodium sulfadiazine used in this study were furnished by the Lederle Laboratories, Inc.

in the toxic effects of the three drugs was to be found in the incidence of vomiting, which was present in 20.5 per cent of the patients treated with sulfapyridine, in 5.9 per cent of those receiving sulfathiazole and in 1.4 per cent of the patients given sulfadiazine. These differences are statistically significant. The frequency of vomiting in our series was less for all three drugs than that found by other investigators. This is probably due to the high proportion of Negro to white patients in our series (more than 2 to 1). An analysis of our patients treated with sulfapyridine showed that vomiting occurred in 37.6 per cent of the white patients and in only 20.2 per cent of the Negroes receiving this drug. It is our experience that the same relationship holds for the other sulfonamides also.

The presence of a renal calculus was diagnosed when gross hematuria, anuria or pronounced unexplained oliguria, pain over the kidneys or ureters or any combination of these was encountered. Neither the presence of sulfonamide crystals in the urine nor microscopic hematuria was considered indicative of the presence of a calculus, since these elements are present in the urine of a great many patients receiving the sulfonamide drugs under consideration. Using the criteria that have been named for diagnosis, we found kidney stones in 1.6 per cent of the patients receiving sulfapyridine, 2.8 per cent of those receiving sulfathiazole and 1.5 per cent of those receiving sulfadiazine. These cases will be discussed later in more detail.

We have placed in one group all the patients with fever, dermatitis and conjunctivitis (or episcleritis) resulting from the use of the sulfonamides, since these complications often occur simultaneously and since all three phenomena are apparently due to a similar type of sensitivity to these drugs. The incidence of these reactions following sulfapyridine and sulfadiazine was relatively low, 2.4 and 2.0 per cent respectively, as compared with 6.2 per cent in the patients receiving sulfathiazole. These differences are significant by the chi square test when the reactions following sulfathiazole are compared with those following sulfapyridine or sulfadiazine but not in the case of sulfapyridine as compared with sulfadiazine.

In the presence of a severe infectious disease, disorientation and mental confusion resulting from the use of drugs is difficult to evaluate. Nevertheless, after studying this symptom carefully in its time relationship to sulfonamide administration we are reasonably certain that these drugs contributed to the presence of mental confusion in 2.4 per cent of the patients receiving sulfapyridine, in 1.6 per cent of those given sulfathiazole and in 1.5 per cent of those to whom sulfadiazine was administered. These differences are not statistically significant.

The incidence of hematologic complications was not especially different for any of the three drugs except for the occurrence of 7 cases (1.4 per cent) of acute hemolytic anemia following sulfapyridine and only 1 each following sulfathiazole and sulfadiazine (0.3 and 0.2 per cent respectively). Leukopenia with a drop in the white blood cells below 4,000 per cubic millimeter was observed in 6 patients (1.2 per cent) receiving sulfapyridine, in 4 (1.2 per cent) receiving sulfathiazole and in 6 (0.9 per cent) receiving sulfadiazine. Granulopenia in addition to the neutropenia occurred in 4 of these sulfapyridine treated patients, in 2 of the sulfathiazole treated patients and in 3 of the sulfadiazine treated patients. The only difference which is significant in the aforementioned group is the higher incidence of acute hemolytic anemia following sulfapyridine as compared with that following the other two drugs.

A definite leukocytosis, independent of the disease for which treatment was being given, developed in 2 patients to whom sulfadiazine was administered. There were increases in the leukocyte counts to 57,000 and 63,700 respectively and an increase in the mature polymorphonuclears and band forms. These counts returned to normal within three days after the cessation of sulfadiazine therapy.

Less frequent toxic complications were yellow vision in 1 patient who received sulfathiazole and 1 who received sulfadiazine and peripheral neuritis in 1 patient who was given sulfapyridine. This case has been reported elsewhere by Sugar.[3]

TABLE 1.—*Toxic Reactions Following the Administration of Sulfapyridine, Sulfathiazole and Sulfadiazine*

Toxic Reaction	Sulfapyridine		Sulfathiazole		Sulfadiazine	
	No. of Patients	Per Cent	No. of Patients	Per Cent	No. of Patients	Per Cent
Vomiting	102	20.1	19	5.9	9	1.4
Renal calculus	8	1.6	9	2.8	10	1.5
Drug fever, dermatitis and/or conjunctivitis	12	2.4	20	6.2	13	2.0
Mental confusion	12	2.4	5	1.6	10	1.5
Leukopenia (with or without granulopenia)	6	1.2	4	1.2	6	0.9
Acute hemolytic anemia	7	1.4	1	0.3	1	0.2
Leukocytosis	0	0	0	0	2	0.3
Yellow vision	0	0	1	0.3	1	0.2
Peripheral neuritis	1	0.2	0	0	0	0
Total patients with toxic reactions	149	29.4	58	11.8	51	7.7
Patients with no toxic reactions	359	70.6	263	88.2	609	92.3
Total patients treated	508	100.0	321	100.0	660	100.0

RENAL CALCULI

The symptoms which led to the diagnosis of sulfonamide calculus in our patients were pain over kidneys and/or ureters in 7 cases, gross hematuria in 6, gross hematuria and kidney pain in 4, anuria or definite oliguria in 3, anuria and kidney pain in 3 and oliguria and gross hematuria in 2. The condition of 1 other patient was not diagnosed during life. This patient showed nothing suggestive of a calculus except nitrogen retention and microscopic hematuria, but after death from endocarditis she was found to have a sulfadiazine calculus in the pelvis of one kidney. The only other death in this group was of a patient with a pneumococcic pneumonia who died following the formation of a sulfathiazole calculus. The death of each patient was attributable to the original disease and not to the kidney stone.

The symptoms of calculus formation began anywhere from the first to the tenth day of treatment. Every patient who developed calculi had received doses of the drug of 1 Gm. or more every four hours, sometimes supplemented by the sodium salt intravenously, and every patient was either dehydrated before treatment began or received insufficient fluids in proportion to the dose of the drug given. Calculi were particularly likely to occur in patients who were being treated for

3. Sugar, S. J.: Peripheral Neuritis Following the Administration of a Glucose Sulfapyridine Compound, New England J. Med. **226**: 1021-1022 (June 25) 1942.

meningitis or endocarditis, because these patients were often given large amounts of the drugs so that high blood levels might be maintained. Among the 82 patients receiving sulfadiazine for meningitis or endocarditis, 5 (6.1 per cent) developed renal calculi, while among the remaining 578 patients who were given sulfadiazine for other illnesses the 5 patients who developed calculi represented only 0.9 per cent of all the patients treated. Nine patients with meningitis or endocarditis were given sulfapyridine and 1 (11.1 per cent) developed a calculus. Among the remaining 499 patients who received sulfapyridine 7, or 1.4 per cent, developed calculi. Only 4 patients received sulfathiazole for the treatment of endocarditis or meningitis. None of these developed calculi. Among the 317 patients receiving this drug for other diseases 9, or 2.8 per cent, developed calculi.

When all the patients developing calculi are considered, with the exception of those treated for meningitis and endocarditis, the difference between the sulfadiazine and sulfathiazole treated groups is the only one which is significant.

excessively or is already dehydrated at the start of treatment, the urinary output may become too small to keep the crystals in solution.

Brown, Thornton and Wilson [4] showed that the higher the level of sulfapyridine in the blood the greater was the possibility of calculi being formed. From table 2 it will be seen that this same relationship holds in our patients treated with sulfapyridine, sulfathiazole and sulfadiazine. Among 117 patients whose maximum free blood sulfonamide levels were between 1 and 3.9 mg. per hundred cubic centimeters none developed renal calculi. In the groups of patients whose highest free sulfonamide levels were 4 to 6.9 or 7 to 9.9 mg. per hundred cubic centimeters there were 1.1 and 1.3 per cent of the patients respectively who developed renal calculi. Among the 290 patients whose highest free blood sulfonamide level was 10 mg. or more per hundred cubic centimeters 10, or 3.4 per cent, developed calculi. It is also interesting that, whereas 3 patients whose free blood sulfapyridine levels were between 4 and 6.9 mg. per hundred cubic centimeters developed calculi, no patients with these maximum levels following

TABLE 2.—*Incidence of Renal Calculi in Patients Treated with Sulfonamides According to the Highest Blood Level Attained*

		Highest Blood Level Attained									
		1-3.9 Mg. per 100 Cc.		4-6.9 Mg. per 100 Cc.		7-9.9 mg. per 100 Cc.		10 Mg. per 100 Cc. and Above		Total	
Drug Used		Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent
Sulfapyridine.....	Patients with calculi.....	0	..	3	3.5	1	1.3	2	3.0	6	2.0
	Total patients.....	64		85		77		71		297	
Sulfathiazole.....	Patients with calculi.....	0	..	0	...	1	5.0	3	15.0	4	2.7
	Total patients.....	31		77		21		20		149	
Sulfadiazine.....	Patients with calculi.....	0	..	0	...	1	0.7	5	2.5	6	1.3
	Total patients.....	22		117		137		199		475	
All drugs.....	Patients with calculi.....	0	..	3	1.1	3	1.3	10	3.4	16	1.7
	Total patients.....	117		279		235		290		921	

The treatment given 20 of the 26 patients with calculi was merely the discontinuance of the offending sulfonamide and the forcing of fluids. Three patients who had been treated with sulfathiazole and the 1 who had been given sulfadiazine required cystoscopy with catheterization and lavage of the ureters. One of these patients with a sulfathiazole calculus required this procedure twice. It was effectual in starting the urinary flow in all cases. The disease of 1 patient with renal colic during the treatment of meningococcic meningitis with sulfadiazine was considered more serious than the complication, and the drug was continued while fluids were given at the rate of 5,000 cc. a day. The pain disappeared and no further symptoms occurred during the remainder of the sulfadiazine therapy. As stated before, 1 patient died in whom the calculus was not diagnosed and who consequently received no treatment for it.

The formation of renal calculi is a serious and sometimes lethal complication of sulfonamide therapy. The mechanism is the crystallization of the sulfonamide or its acetyl derivative in the pelvis of the kidneys, ureters or collecting tubules. The urinary flow is diminished or stops completely, nitrogen retention develops and death may ensue unless the obstruction is removed. If fluid intake and consequently fluid output through the kidneys is sufficient to keep these crystals in solution, calculi will not form. If the fluid intake is insufficient or if the patient is vomiting, has diarrhea, is sweating

sulfathiazole or sulfadiazine therapy developed calculi. In the sulfathiazole treated group no patients developed calculi unless their maximum free blood sulfathiazole levels were 7 mg. or more per hundred cubic centimeters. In the sulfadiazine treated group none developed unless the corresponding blood sulfadiazine levels were 9.2 or more.

It is apparent that when the intake, and consequently the blood levels and urinary output, of the sulfonamides are kept low, renal calculi occur rarely if at all. This is borne out by the fact that, among the 182 patients whom we have treated with sulfadiazine in doses of 0.5 Gm. or less every four hours there has not been a single instance of renal calculus formation. The same is true for the 43 patients receiving sulfathiazole in similar low doses.

Our observations indicate that sulfadiazine administered in these low doses is as effective against pneumococcic pneumonia as when 6 Gm. a day is given.[5] We have now treated 123 patients with pneumococcic pneumonia in this way, with eleven deaths, or a 9 per cent case fatality rate. This compares favorably with our results and those of others in the treatment of pneumococcic pneumonia with higher doses of sulfa-

4. Brown, W. H.; Thornton, W. B., and Wilson, J. S.: An Evaluation of the Clinical Toxicity of Sulfanilamide and Sulfapyridine, J. A. M. A. **115**: 1605-1611 (April 27) 1940.

5. Dowling, H. F.; Hartman, C. R.; Feldman, H. A., and Jenkins, F. A.: The Comparative Value of High and Low Doses of Sulfadiazine in the Treatment of Pneumococcic Pneumonia, Am. J. M. Sc. **205**: 197-203 (Feb.) 1943.

diazine.[6] If further observations confirm our findings, the administration of these smaller doses should be the optimal way to treat patients with pneumococcic pneumonia.

The other method of preventing renal calculi following sulfone treatment is to give sufficiently large amounts of fluids to insure an adequate renal output no matter how high the dosages of the drug. In every case in which a sulfonamide calculus occurred among our patients, the patient was dehydrated or took insufficient fluids after therapy began, or a large intravenous dose of the sulfonamide had been given without sufficient fluids to take care of adequate renal output. We recommend a total of 3,000 cc. of fluids a day for patients receiving the sulfonamides, or enough fluid to insure a urinary output of at least 1,200 cc. a day. We have been able in several instances to give sufficient sulfadiazine to keep the free blood sulfadiazine level constantly at 20 mg. per hundred cubic centimeters or above, without evidence of renal calculus formation, by giving large amounts of fluids at the same time. The proper relationship between fluids and sulfonamide intake is the key to the prevention of calculi.

DERMATITIS, CONJUNCTIVITIS AND DRUG FEVER

In table 3 are shown the cases of dermatitis, conjunctivitis and/or drug fever encountered by us. Since reactions following second and successive courses of the sulfonamides are included in this table, the totals are greater than those in table 1, which includes only the first courses of the three sulfonamides. Sulfathiazole was responsible for a larger number of these reactions than either of the other drugs, and the reactions were more varied in type when they followed sulfathiazole. While sulfapyridine caused only maculopapular rashes and sulfadiazine both maculopapular and erythematous (scarlatiniform) types, sulfathiazole therapy was followed by 3 erythematous, 4 maculopapular, 7 nodular, 1 urticarial and 1 petechial rash. In patients receiving the first course of a sulfonamide, the onset of the rash occurred between the second and sixteenth day of treatment with the drug, nearly two thirds occurring between the sixth and tenth days. In the patients developing rash or fever following the second course of sulfathiazole, the reaction in 1 patient began on the third day of the second course, in other patients on the fourth, fifth and seventh days, while 1 patient developed a rash with itching two hours after the first dose of the second course was taken.

Leukocyte counts during the height of the rash, drug fever or conjunctivitis ranged from those within normal limits to one which reached 64,700 per cubic millimeter, the majority being below 14,000, however. In the cases of conjunctivitis without dermatitis there was no leukocytosis unless drug fever was also present. In no instance was there an eosinophilia.

In every case the rash and fever subsided within four days after the cessation of sulfone therapy. The fact that no cases of exfoliative dermatitis occurred may be attributed, for the most part at least, to the fact that sulfonamide therapy was stopped promptly as soon as the rash appeared.

HEMATOLOGIC COMPLICATIONS

In all of the cases of leukopenia which developed, the leukocytes remained above 3,000 per cubic millimeter except in 1 patient, in whom they reached 2,340 per cubic millimeter at the lowest level. The onset of leukopenia occurred anywhere from the third to the sixteenth day of sulfonamide treatment. There was no case of agranulocytosis in the series, a fact which may have been due to prompt detection of the abnormality in its milder stages and immediate discontinuance of the sulfonamide. In many instances the leukocyte count was again within normal limits on the day following discontinuance of sulfonamide therapy, although in the majority of cases a longer interval was required, the longest being six days.

An acute hemolytic anemia with a drop of 1 million or more red blood cells, occurred in 7 patients receiving sulfapyridine and in 1 each receiving sulfathiazole and sulfadiazine. These anemias began on the second to the seventh day following the commencement of treatment. Sulfonamide therapy was discontinued promptly in every case, but the erythrocyte counts remained low and in some cases continued their downward courses. In 1 patient the red blood cells reached 1,700,000 per cubic millimeter with a hemoglobin of 34 per cent and the patient died, presumably as a result of his pneumonia and the added burden of the anemia. In most instances transfusions were employed to bring the red blood cells up to normal levels, although they usually rose slowly without this assistance.

TABLE 3.—*Dermatitis, Conjunctivitis and Drug Fever Following Sulfonamide Therapy*

	Sulfapyridine	Sulfathiazole	Sulfadiazine
Complication			
Dermatitis alone	5*	7†	5*
Conjunctivitis alone	0	3	0
Drug fever alone	3	5	5
Dermatitis and conjunctivitis	0	1‡	0
Dermatitis and fever	4	6	5
Conjunctivitis and fever	0	3	0
All three complications	0	2	0
Total	12	27	15
Type of rash			
Erythematous or scarlatiniform	0	3	3
Maculopapular or morbilliform	9	4	6
Nodular	0	7	0
Urticarial	0	1	1
Petechial	0	1	0

* Two had fever from disease. † Four had fever from disease.
‡ Fever present from the disease.

AGE AND SEX DISTRIBUTION OF TOXIC REACTIONS

We have computed the relative number of toxic reactions occurring in males as compared with females. There was no significant difference in the percentage of any of the toxic effects in the two sexes with the exception of vomiting. This occurred more than twice as frequently in females as in males, regardless of the drug used. It was present in 15 per cent of the male patients receiving sulfapyridine and in 33.5 per cent of the females. The corresponding figures for sulfathiazole were 5.2 and 11.3 per cent and for sulfadiazine 1.2 and 3.1 per cent.

There was no apparent difference in the number of toxic reactions in the various age groups, although

6. Dowling, H. F.; Hartman, C. R.; Sugar, S. J., and Feldman, H. A.: The Treatment of Pneumococcic Pneumonia with Sulfadiazine, J. A. M. A. **117:** 824-826 (Sept. 6) 1941. Ensworth, H. K.; Kalkstein, Mennasch; Barefoot, S. W.; Liebmann, James, and Plummer, Norman: Sulfadiazine in Pneumonia: Treatment in 239 Cases, Am. J. M. Sc. **204:** 179-185 (Aug.) 1942. Finland, Maxwell; Strauss, Elias, and Peterson, O. L.: Sulfadiazine: Therapeutic Evaluation and Toxic Effects on 446 Patients, J. A. M. A. **116:** 2641-2647 (June 14) 1941. Flippin, H. F.; Rose, S. B.; Schwartz, Leon, and Domm, A. H.: Sulfadiazine and Sulfathiazole in the Treatment of Pneumococcic Pneumonia, Am. J. M. Sc. **201:** 585-592 (April) 1941.

the lowest age group was poorly represented, there being only 33 patients under 10 years of age in the entire study.

COMMENT

Although the sulfonamides have been used extensively for several years and nearly every physician has had some experience with them, nevertheless there is no common agreement as to the seriousness of their toxic effects. It is the common practice of many physicians to use them in a great variety of diseases, even when the indications for their use are not specific (or, indeed, very clear), since these drugs have, as they say, practically no toxic effects. On the other hand, many physicians, particularly those who have seen fatalities attributable to these drugs, believe that they may cause serious or fatal complications even under the most careful regulation of treatment and observation of the patient. We believe that the figures which we have presented do not support either of these extreme views. We have shown that toxic reactions occur following the use of sulfapyridine, sulfathiazole and sulfadiazine, in descending order of frequency, but that the serious complications are few in number when the patients are watched closely, when the drugs are stopped promptly if reactions occur, and especially when sulfadiazine is used. Only 3 patients in the entire group died at a time when a complication of sulfonamide therapy was present. In 2 of these who had renal calculi the deaths were unquestionably due to the diseases for which the sulfonamides were being given. In the third patient, who developed acute hemolytic anemia in the course of sulfapyridine therapy for pneumonia, death may have been contributed to by the drug reaction. Thus it is seen that 1,564 courses (including second and later courses) of the sulfonamides were administered to a large group of patients, for the most part under the conditions which exist in a city hospital, with a minimum of serious toxic reactions and only one fatality which might have been due in part to the sulfonamide administered.

The question of how best to avoid toxic reactions is best answered in two parts. First, renal calculi may be avoided by the use of sulfadiazine in preference to sulfathiazole and sulfapyridine, and by preserving the proper balance between the amounts of drug and fluids given. When good results can be expected from the treatment of a disease with relatively small doses of a sulfonamide, as we have shown to be the case with sulfadiazine in pneumococcic pneumonia, this method of avoiding renal calculi should be taken. When larger doses are needed they can be used without the formation of calculi if careful attention is paid to fluid intake and output.

Secondly, with regard to other complications, vomiting is almost completely absent when sulfadiazine is used, while the chances of producing drug fever, dermatitis, anemia and leukopenia following sulfadiazine therapy are either the same as or less than if other sulfonamides are used. Even with sulfadiazine a few toxic reactions of this sort will nevertheless occur. Serious and fatal results can be almost completely prevented by having blood counts taken every other day and by careful examination of the patient every day and by discontinuing the drug promptly if toxic reactions appear. We believe that in the light of present knowledge only by the use of the measures outlined can sulfonamides be given with the maximum of safety to allow them to be properly used in all cases where they are needed to achieve their full therapeutic effects.

SUMMARY AND CONCLUSIONS

1. Sulfapyridine was administered to 498 patients with toxic effects in 29.9 per cent, sulfathiazole to 321 patients with toxic effects in 11.8 per cent and sulfadiazine in 660 patients followed by toxic reactions in 7.7 per cent. Detailed analysis was made of the toxic reactions encountered in the use of each of these drugs.

2. Renal calculi were found least frequently in patients treated with sulfadiazine or sulfapyridine. Their frequency varied in direct proportion to the maximum level of free sulfonamide in the patient's blood. None occurred in patients given 0.5 Gm. of sulfadiazine or sulfathiazole every four hours or less. When larger doses of these drugs were given, renal calculi occurred when fluid output was diminished for some reason.

3. Blood dyscrasias occurred less frequently following sulfadiazine and sulfathiazole. The only death in the entire series which might be partly attributable to sulfonamide therapy occurred in a patient with acute hemolytic anemia following sulfapyridine therapy.

4. The optimal therapy for most infectious diseases at the present time involves the use of sulfadiazine, in low doses whenever possible but in high doses when necessary, provided there is careful regulation of fluid intake and output and frequent blood counts and urinalyses, combined with close observation of the patient.

THROMBOCYTE DEFICIT

THE BEHAVIOR OF THE BLOOD PLATELETS IN DISEASES OF VASCULAR STASIS OF THE EXTREMITIES

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This report is rather incomplete in its data and conclusions because the two years in which I have been collecting cases have not permitted the detailed anatomic and physiologic searchings that seem indicated. However, I feel that in these days of marching feet any research that will contribute to our knowledge of the circulation of the lower extremities is worth while. The basis of this study has been a comparison of the platelet counts on blood taken from the ear of patients with circulatory diseases of the legs with counts on blood taken immediately from the right and the left foot.

If the circulation of blood is sufficiently slowed or otherwise becomes incompetent in an extremity and thereby reduces the nutrition of an area to a point of tissue damage, certain phenomena will occur. These phenomena are dependent on failure of oxygen supply and failure of removal of carbon dioxide and catabolic products. The result is a disturbance of normal cell function, accumulation of fluid and of serum proteins, inflammation and finally tissue death. Within these areas the blood vessels suffer as a part of the processes of decompensation. The vasa vasorum fail to keep up a healthy state of nutrition, and vascular tone is lost. With this loss of tone dilatation occurs, and the blood flow is further slowed. As the blood in the large veins becomes further charged with carbon dioxide and waste products, damage to the intima appears.

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With this slowing of the blood flow the thrombocytes drop from the axial stream and adhere to areas of intimal damage, and white thrombi form. Partial thrombocyte disintegration occurs in these thrombi, and the products of the dissolution enter the blood stream in increasing concentration.

If one accepts the observations of Ceder, Zon and Crigler,[1] who demonstrated rather competently that thrombocytes are the main and probably the sole vehicles for histamine in the circulating blood, one can recognize the role that this potent substance must play in the development of the sensitization of the skin.

This is the picture of circulatory stasis disease of the lower extremities the result of which is edema, dermatitis and ulceration—also pigmentation and hemorrhage and accumulation of serum protein in extravascular areas. The dermatitis may not be confined to the area of stasis alone but, owing to the catabolites acquired through disturbed nutrition and cellular disintegration, may develop on other areas of the body, most usually on those areas exposed to light. The solar sensitivity of the patient with varicose dermatitis is well known. The other products of disturbed cellular metabolism with changes in hydrogen ion concentration are likewise to be considered a source of trouble but are not investigated in the development of this paper.

The accidental observation that thrombocytes were definitely diminished within the capillaries of the feet of persons who suffered from chronic stasis diseases of the leg and of those with lichen chronicus simplex of the same areas led to a procedure which I have designated the "thrombocyte deficit" test. The results of this test in more than 200 cases have helped me to construct a picture of the degree of damage suffered by an extremity from such stasis and occasionally predict its chances of repair. This has been useful in the clinical management of cases presenting involvement of the leg. I reported a smaller series of cases before the dermatologic section of the California Medical Association in May 1940. This paper was not published and has been developed to include the larger studies in the present paper.

Something should be said regarding the origins and behavior of blood platelets that are definite problems in an investigation of this type.

1. Platelets may be formed from the breaking up of megakaryocytes but may be caused to clump together again only to break apart a second time and reform as individuals within the course of a few minutes. This suggests that the platelets in the cases considered are not undergoing dissolution; however, the reduction of the ear count considerably below normal in long standing cases indicates an actual loss of the platelet itself.

2. Platelets may fragment into smaller forms while passing through capillaries. This presumably gives an apparent increase in count in some circumstances; a skilful technician will avoid this pitfall, however.

3. Agglutination of platelets may be precipitated by a slight modification of plasmatic equilibrium. Agglutination is lessened by experimental asphyxia and in anaphylactoid purpura. We would therefore expect a lessened agglutination in these affected legs, for asphyxia is certainly present.

4. The distribution of platelets in the vessels of different organs varies widely. There are variations in parts of the circulation or even in the same vessel at the same time: showers of platelets appear, only to be followed by an extreme scarcity within a short interval. Vasomotor changes, stagnation or agglutination occurs frequently. Tocantins [2] found that the number of platelets in arterial blood of the upper extremity was significantly higher than in venous or cutaneous blood. This was not true of the erythrocytes. The taking of the several counts should therefore be done within a short time of each other. The consistency of the findings by repetition in the same case indicates that a reasonable constancy of count can be expected.

5. Seasonal variation, time of day, activity, menstruation, digestion, age, race, posture, temperature, altitude, pregnancy and various diseases may be lumped together as other factors of definite influence on the counts.

It is our object in this paper to present as a preliminary report a method of comparison of platelet

TABLE 1.—*Platelet Counts in a Series of Twenty Cases*

Case	Sex	Age	Platelet Counts, Thousands	Description of Pathologic Condition
1. C. J. L....	♀	45	Ear..... 120 Right foot. 83* Left foot.. ..	*Eczematoid eruption of ankle, epidermophytosis
2. W. E. P..	♂	68	Ear..... 178 Right foot. 64* Left foot.. 138	*Sclerosis and ulcer, varicose dermatitis
3. G. E.....	♂	63	Ear..... 148 Right foot. 83' Left foot.. 68*	'Slight chronic edema *Heavy woody edema, dermatitis, varicosities
4. W. M. C..	♂	56	Ear..... 310 Right foot. 81* Left foot.. 68*	*Itching of both ankles, edema and punctate pigmentation of both ankles
5. K. E. A...	♂	35	Ear..... 166 Right foot. 164 Left foot.. 92*	*Old ulcer, punctate hemorrhages, pigmentation
6. J. B.....	♂	58	Ear..... 240 Right foot. 74* Left foot.. 144*	*Hemorrhagic lesions of both legs and ankles; no edema
7. H. P.....	♂	35	Ear..... 172 Right foot. 126' Left foot.. 71*	'Edema mild *Ulcer and stasis
8. C. W..... (See 9) 12/29/38	♂	78	Ear..... 245 Right foot. 186* Left foot.. 213'	*Ulcer 'Scaly edema
9. C. W..... 12/29/39	..	..	Ear..... 158 Right foot. 144' Left foot.. 118*	'Healed *Ulcer and sclerosis
10. C. J. H...	♂	39	Ear..... 144 Right foot. 102' Left foot.. 60*	'Schamberg's disease mild *Schamberg's disease definite eruption
11. F. J. W..	♂	75	Ear..... 242 Right foot. 178' Left foot.. 86*	'Moderate lichenification *Severe lichenification, amyloidosis
12. M. F.....	♂	55	Ear..... 215 Right foot. 174 Left foot.. 116	Contact dermatitis (wool) of both legs resistant to treatment
13. S. J.....	♂	65	Ear..... 118 Right foot. 58* Left foot.. ..	*Lichen chronicus simplex
14. D. B.....	♂	32	Ear..... 151 Right foot. 46* Left foot.. 134'	*Thick lichen simplex ankle 'Normal leg
15. R. M. T..	♂	62	Ear..... 114 Right foot. 86* Left foot.. 96'	*Varicose dermatitis and edema 'Varicose veins
16. A. R. T...	♀	50	Ear..... 205 Right foot. 99* Left foot.. ..	*Punctate hemorrhages
17. F. F. M..	♂	48	Ear..... 122 Right foot. 66* Left foot.. ..	*Lichen planus hypertension, edema
18. A. S. C...	♂	78	Ear..... 186 Right foot. 56' Left foot.. 36*	'Varicosities *Sclerosis and pigmentation, edema
19. P. J. W..	♀	38	Ear..... 210 Right foot. 146* Left foot.. 136*	*Erythema induratum of both legs
20. E. P.....	♀	45	Ear..... 206 Right foot. 160' Left foot.. 86*	'Slight varicose *Ulcer, varicose veins, edema

* Indicates leg of chief complaint.
' Indicates leg of secondary symptoms.

1. Zon, Leo; Ceder, E. T., and Crigler, Catherine W.: The Presence of Histamine in the Platelets of the Rabbit, Pub. Health Rep. **54**: 1978 (Nov. 3) 1939.

2. Tocantins, L. M.: Proc. Physicl. Soc., Philadelphia, Am. J. M. Sc. **192**: 150, 1936.

counts on a person at relatively the same time and under the same conditions.

This method gives first a survey of anatomically extreme areas of cutaneous vessels which will indicate any general abnormality of platelet count and at the same time indicate with fair degree of certainty a localized change.

TABLE 2.—*Low Platelet Counts in Series of Sixty-One Cases in 1939*

Number of cases studied		61
Number of cases with counts in one extremity below 100,000	20	
Number of cases with counts in one or both extremities above 100,000 and below 150,000	35	
Number of cases with low counts in ear and both extremities	3	
Total cases with low counts	58	
Number of cases with approximately normal counts	3	
		61

Although variations of platelet counts in extremities relative to postural changes are discussed by Tocantins,[3] a search of the literature has not disclosed any similar investigation. Other studies and reports of changes in the circulatory blood in areas presenting cutaneous disease have been made and reported by Kovács,[4] Piscane,[5] Helmrich,[6] Ratschow,[7] David [8] and Knott and Pearson.[9]

Kovács compared the local blood picture in the presence of different cutaneous diseases with finger blood in 50 cases. He investigated the changes in the blood cell counts in the location of the disease. The neutrophils, eosinophils, basophils, monocytes and lymphocytes were studied in 6 cases of psoriasis, 5 cases of erythema induratum, 6 cases of erythema multiforme, 6 cases of urticaria, 3 cases of prurigo, 2 cases of pityriasis rosea, 5 cases of chronic eczema, 2 cases of lichen ruber planus, 4 cases of dermatitis herpetiformis, 4 cases of dermatitis artificialis, 2 cases of arsphenamine dermatitis and 1 case each of neurodermatitis, erythema elevatum diutinum, mycosis fungoides and parapsoriasis.

Analysis of this study shows that in only the chronic type of lesion was there any variation in the blood cell counts. Evanescent or noninfiltrative diseases such as urticaria and pityriasis rosea showed no change in cellular types. The cases are too few in number for practical interpretation.

Piscane found that the venous pressure was elevated in all forms of varicosities. Capillary pressure was normal.

Helmrich directed attention to the blood picture in the pathologic cutaneous area "in loco" by examining the blood in the papule of a tuberculin reaction and found an increase in the lymphocytes.

Ratschow examined the blood flow in diseased extremities my means of roentgen rays.

David compared blood taken from the finger tip, as did Kovács, with the blood of a pathologic cutaneous area and concluded that, as would be expected, there was a fixed deviation in the proportion of the local blood structure and the foreign (finger tip) picture. The search was not sufficiently followed to develop a method for differential diagnosis.

Knott and Pearson found increases in eosinophils following the injection of histamine or proteins in sensitized persons.

These studies which compare finger tip blood with lesion blood show that such blood cell changes are found, as might be expected, in lesions that show similar alterations in a biopsy; they do not give an index of changes dependent on blood velocity and nutritional damage. I believe that it will readily be seen that the studies are not comparable. Furthermore, reference to the thrombocytes has not been found in these reports.

A series of 20 cases is presented for the purpose of illustration in table 1, and a summary of 61 cases collected in 1939 is given in table 2. Table 3 shows the distribution of the counts according to the clinical results and table 4 the distribution of the pathologic condition in relation to the counts.

In 2 cases finger counts were done in addition to the others. The finger blood corresponded to the ear count in these cases, so that I did not continue the practice. This is further borne out by numerous relatively normal counts on blood taken from the leg of persons not exhibiting any apparent vascular anomaly. Bleeding times were also studied for a while, but when it was found that they gave no significant information they were stopped.

Counts of the white and red corpuscles were also done with a few of the platelet counts, but the variation in these cells was in no wise proportionate to the platelet count. The variations were largely within a normal margin of error.

The venous blood of the dorsalis pedis vein has shown a platelet count comparable to although consistently lower than the ear count. This would seem to indicate that the sharp reduction of platelets in the smaller capillary areas is secondary to the development of a congestive sclerosis. The number of platelets in the

TABLE 3.—*Clinical Correlation of Counts*

		No. of Cases
1. Soft edema and dermatitis		20
Counts below 100,000	6	
Counts below 150,000	9	
Counts below 200,000	3	
Counts above 200,000	2	
2. Sclerosis and woody edema		13
Counts below 100,000	3	
Counts below 150,000	7	
Counts below 200,000	2	
Counts above 200,000	1	
3. Cases of ulcer		18
Counts below 100,000	3	
Counts below 150,000	7	
Counts below 200,000	6	
Counts above 200,000	2	
4. Chronic stasis with pigment (progressive pigmentary dematosis type of Schamberg)		18
Counts below 100,000	6	
Counts below 150,000	8	
Counts below 200,000	0	
Counts above 200,000	0	
5. Ear counts		82
Below 100,000	4	
Below 150,000	9	
Below 200,000	19	
Normal	50	
6. Lichen chronicus simplex (on affected side)		29
Counts below 100,000	9	
Counts below 150,000	14	
Counts below 200,000	4	
Counts normal	2	

3. Tocantins, L. M.: Am. J. Physiol. **119:** 439, 1937.
4. Kovács, Zsigmond: Das örtliche qualitative weisse Blutbild bei verschiedenen Hauterkrankungen, Arch. f. Dermat. u. Syph. **176:** 130-137, 1937.
5. Piscane, C.: Boll. della Sez. Region, April 1932, supplement to Gior. ital. di dermat. e sif.
6. Helmrich: Wien. klin. Wchnschr. **2:** 1679, 1930.
7. Ratschow: Arch. f. Dermat. u. Syph. **177:** 133-147 (May) 1938.
8. David, M.: Ueber das "Lokal Blutbild" der Hautkrankheiten, Dermat. Wchnschr. **109:** 943 (Aug. 12) 1939.
9. Knott, F. A., and Pearson, R. S. B.: Eosinophylia in Allergic Conditions, Guy's Hosp. Rep. **84:** 230 (April) 1934.

vein may result from retrograde circulation which is common in the presence of incompetent venous valves. Some of the platelets also may result from the breaking up of agglutinated groups and by passage through dilatations that amount to minor arteriovenous anastomoses. I am assuming that the finer capillary beds give a relative index of the damage to the tissues themselves. In a portion of these cases tests were taken from the center of sclerosed areas. These counts corresponded closely to the toe counts.

Since these smallest of blood cells are held back when polymorphonuclears and erythrocytes are able to pass through the smaller capillaries, it is probable that they are retained by adherence and dissolution. Their products and the tissue catabolites, therefore, form the waste that accumulates as the vicious circle revolves. The platelet loss in the capillary areas of the skin may explain the purpuric breakdown of the varicose ulcer.

The method of counting used is reported by the collaborating author.

LABORATORY PROCEDURE

Technic.—A drop of freely flowing blood from a deep stab wound, made with a number 11 Bard Parker knife, was obtained from the ear and fourth toe of each foot after a thorough cleansing with 50 per cent ethyl alcohol. This blood was drawn to the 0.5 mark of a certified [10] Thoma erythrocyte diluting pipet, immediately diluted with Rees-Ecker [11] fluid to the 101 mark and shaken vigorously for thirty seconds. The pipet was labeled, capped with a rubber band and placed in the refrigerator at 4 C., unless counted at once. At the time of the counting the pipet was brought to room temperature, shaken by hand for thirty seconds and then by mechanical shaker for five minutes, and the two sides of a certified,[10] improved Neubauer type hemocytometer were correctly filled. After the hemocytometer had stood (in a Petri dish containing moist filter paper) for a period of fifteen minutes, the number of platelets in the center square millimeter of 400 squares was counted on each side of the hemocytometer and the average of these numbers was multiplied by 2,000, giving the number of blood platelets per cubic millimeter of blood. The normal count is 200,000 to 400,000.

Pipets were cleaned after each count by drawing them full of cleaning solution (commercial sulfuric acid saturated with potassium dichromate) and withdrawing after one hour. A quantity of distilled water was then run through them until no trace of acid remained. They were then rinsed with acetone and dried with air by suction. Hemocytometer surfaces were cleaned with cleaning solution, rinsed with distilled water and wiped dry with a soft lintless cloth.

The diluting fluid of Rees and Ecker [11] is prepared by dissolving the following constituents in 100 cc. of distilled water and filtering and refiltering weekly: sodium citrate 3.8 Gm.; formaldehyde neutral, 40 per cent, 0.2 cc.; brilliant cresyl blue 0.1 Gm.

Choice of Technic.—The method used is one that the technologist (N. H.) previously adopted and used for clinical blood platelet counts. When this series of counts was started a critical review of methods was made and this method continued on the basis of accuracy, speed and adaptability to this problem and general clinical use.

10. Certified correct by United States (National) Bureau of Standards.
11. Rees, H. M., and Ecker, E. E.: An Improved Method for Counting Blood Platelets, J. A. M. A. 80: 621 (March 3) 1923.

Use of a direct method was confirmed after consideration of the literature and Tocantins' [12] brief of 116 technics, including that of Olef.[13] Conclusive evidence presented by Tocantins shows that direct methods are more accurate than indirect methods in experienced hands. Volume per cent methods were not used, as they may be 56 per cent in error.[14] A capillary source of blood was essential, as venipuncture would defeat the purpose of the study. Standard certified pipets and hemocytometers are available and adequate.[15] A magnification of 430 diameters using the high dry objective is best, since it avoids errors of overmagnification and undermagnification when continuous use is made of the fine adjustment of the microscope.

Rees-Ecker diluting fluid met all the necessary criteria, since it is isotonic and has an anticoagulant, sodium citrate; a fixative, neutral formaldehyde, to prevent morphologic changes and disintegration of platelets for twenty-four hours; ease of preparation and relative stability without precipitation, and a dye to facilitate counting. The dye may be omitted after some practice or may be added as only 0.05 per cent brilliant cresyl blue. Prewetting of the pipet with diluting fluid by the method of Wright and Kinnicutt [16] was found unnecessary in a series of 10 control counts.

TABLE 4.—*Correctness of Diagnosis Based on Platelet Counts*

	Cases	Per Cent
Distribution (right or left leg) of disorder correctly indicated by low count	61	75.4
Distribution not correctly indicated	10	16.4
Normal counts found in	5	8.2
	76	

Finally our purpose in this series was to obtain comparative blood platelet counts, and since the identical technic was used throughout the relationship of the counts from the various sources is valid, even if the absolute number of platelets would vary with another method.

Checks on Technic.—Five clinically normal persons were rechecked first, then 3 with thrombopenic purpura and 3 with thrombocytosis, all values being within expected limits and confirmed by gross correlation with Wright's stained coverslip smears. For the first 41 counts, including the foregoing, two pipets were filled from each source and the two values checked within 10,000 or plus-minus 2.5 per cent. The same check was obtained against three other technologists using this method. During the series repeat counts were made at brief intervals on the same patient and found to fall within the 2.5 per cent variation. Needless to say, all recorded counts checked within 1 per cent on the values obtained from the two sides of the hemocytometer. If the first preparation did not check, another was made.

That the method is accurate and usable is confirmed by the recently published results of 126 preliminary and 1,034 final counts made by Pohle [17] and a technician at the Harvard School of Medicine using the direct method. The same technic is used in New York,[18]

12. Tocantins, L. M.: Technical Methods for the Study of Blood Platelets, Arch. Path. **23**: 850 (June) 1937.
13. Olef, Isadore: Blood Platelets: An Improved Indirect Method for Their Enumeration, Arch. Int. Med. **46**: 585 (Oct.) 1930.
14. Olef, Isadore: J. Lab. & Clin. Med. **23**: 166 (Nov.) 1937.
15. Tocantins: Technical Methods, p. 857.
16. Wright, J. H., and Kinnicutt, Roger: New Method of Counting the Blood Platelets for Clinical Purposes, J. A. M. A. **56**: 1457 (May 20) 1911.
17. Pohle, Frederick J.: Am. J. M. Sc. **197**: 40 (Jan.) 1939.
18. Paddock, F. K., and Smith, K. E.: Am. J. M. Sc. **198**: 372 (Sept.) 1939.

London [19] and Uppsala,[20] with consistent results. That the method is superior to the "true indirect" technic of Olef [21] is indicated by his own high values and the variable normals [22] (328,000 to 1,206,000) of experienced workers using Olef's method. Finally, Tocantins' [23] last comprehensive treatise again confirms use of the direct method, even with cutaneous blood.

GENERAL CONSIDERATIONS

Since the first question to arise is bound to be one of laboratory error, the checks on the method are given by the collaborating author, and I believe them to be adequate. Furthermore, the close correlation of the three diverse counts on normal persons has shown any significant error to be largely absent. The further agreement of the findings with the distribution of the disease signifies that actual changes have taken place. Both of us have repeatedly been able to indicate the extremity having pathologic conditions from the counts made, even though the side was otherwise unknown. I have also in several instances found changes developing on the patient's "good side" when a low count has indicated damage. In 1 case subsequent ulceration developed in an untreated leg having a low count, although the treated one had long been healed.

TABLE 5.—*Responses of Platelet Counts to Treatment (Ascorbic Acid and Support)*

	Before Treatment		Interval	Subsequent Count
1. H. D.....	Ear.....	175	8 weeks	300
	Right foot....	162		298
	Left foot.....	170		270
2. D. K.....	Ear.....	96	3 weeks	194
	Right foot....	96		124
	Left foot.....	94		102
3. C. H.....	Ear.....	144	4 weeks	176
	Right foot....	102		168
	Left foot.....	60		153
4. F. W.....	Ear.....	240	12 weeks	394
	Right foot....	178		276
	Left foot.....	86		152

The low ear counts in many of these cases raises an interesting speculation, and that is "Does platelet loss in a damaged area exceed platelet production in a sufficient amount to depress the normal total count? If one system continually filters out the platelets from the circulating blood, does the whole circulatory structure suffer?" That this does happen is suggested by the lowered ear counts in long-standing cases.

Another problem is "How low may a platelet count fall before tissue breakdown occurs?" Tocantins [24] states "Spontaneous bleeding into the skin and mucous membranes often appears when the platelets in cutaneous blood drop below 50,000 per cubic millimeter and disappears when they return to normal."

Petechial tests have also been done in 2 cases, with positive results relative to the concentration of the platelets. It would be interesting if it could be shown that a local scurvy is responsible for damage to the blood vessels.

19. Rowlands, R. A., and Vaizey, J. M.: Lancet **2**: 1217 (Nov. 26) 1938.
20. Kristenson, A.: Studien über die Anzahl der Blutplättaschen beim Menschen, Akademische Abhandlung, Uppsala, Appelbergs Boktryckerie Aktiebolag, 1924.
21. Olef, Isadore: J. Lab. & Clin. Med. **20**: 416 (Jan.) 1935.
22. Lee, Pearl, and Erickson, Betty Nims: J. Lab. & Clin. Med. **24**: 821 (May) 1939.
23. Tocantins, L. M.: Medicine **17**: 199 (May) 1938.
24. Tocantins, L. M.: Medicine **17**: 229 (May) 1938.

Since pathologic conditions were indicated in about 4 out of 5 patients examined by a comparison of regional platelet counts, it may be possible on the basis of a thrombocyte deficit for a physician to predict whether or not injection of varicose veins, surgical intervention or other radical procedure can be done without sloughing or failure of success. Furthermore a degree of prognosis should be possible. I believe that my follow-up of these cases justifies the following statements: If the count does not increase within three to six weeks with supporting measures and administration of ascorbic acid in large doses, the prognosis is poor for complete recovery. If the count shows a progressive fall, the prognosis is bad. I feel that in any instance in which there is a low count in an extremity a surgical or an injection procedure not immediately necessary should not be carried out until the thrombocytes have shown a substantial increase.

THERAPEUTIC PROCEDURE

I have routinely applied full elastoplast (Duke Laboratory) bandages for support of the circulation and have administered 200 mg. of vitamin C (ascorbic acid) a day. A few illustrative responses are shown in table 5. Clinical response has paralleled the improvement in the thrombocyte count.

It is important that I am not misunderstood in my use of ascorbic acid. I have not used it in expectation of stimulating platelet production but possibly to aid in the repair of vascular damage. The improvement in the platelet count probably results from an acceleration of the blood flow which keeps the platelets from adhering to the intima. Thus secondary dissolution is avoided. Furthermore, the drain on the rest of the circulation ceases, since platelets are no longer being lost and an increase in the total count results as production again exceeds destruction.

I am not prepared to say whether the circulatory support or the ascorbic acid is responsible, but it is probable that both help. The support permits better maintenance of venous flow, and the ascorbic acid may assist in the vessel repair. Roentgen therapy has been used in some cases to assist in the softening of sclerotic areas or help the healing of eczemas. I have used it sparingly but believe that it has a place in treatment if intelligently used.

COMMENT

This study must be considered a clinicophysiologic experiment. It points out first that tissues are not all bathed alike in a uniform flow of blood constituents. Second, this flow is altered by the withdrawal or dissolution of blood platelets in long-continued slowing of the blood stream in the extremities. This change not only affects the regional blood itself but ultimately results in the lowering of the total number of circulating platelets. The clinical and physiologic conclusions are still hypothetic but, if used as an approximate index of the degree of a pathologic process, are of some clinical importance.

CONCLUSION

Regional diminution of thrombocytes in the circulating blood of capillaries is found in certain diseases of the extremities. The local diminution often parallels the local clinical conditions, the most important of which probably is the vicious circle of vascular stasis. This diminution probably is an indication of the degree of vascular damage. It should have therapeutic and prognostic significance.

241 East Santa Clara Street.

ABSTRACT OF DISCUSSION

DR. THEODORE CORNBLEET, Chicago: Best showed that there are physical changes, such as of the surface tension, which cause the platelets to stick to injured vessels. Injured surfaces too have increased permeability, permitting, no doubt, the smallest formed elements of the blood to escape. It is difficult to show this escape because these elements disintegrate so rapidly. Just what purpose their arrest at the pathologic site serves is not known, but it may be to prevent hemorrhage, since the phospholipid content of platelets induces clotting. They seem also to contain a water soluble material, which acts oppositely on the clotting mechanism inhibiting it. The latter substance may prevent clotting in legs whose tissue becomes diseased. The presence of histamine in platelets would further act to increase permeability, though much recent work ascribes to the eosinophils dominance as carriers of histamine in the blood stream. Zon and others have shown that platelets carry histamine in rabbits' blood. In other species examined, including man, the eosinophils have this function. Accurate and reliable platelet determinations cannot be done easily and routinely in office, clinic or hospital practice, and this difficulty limits procedure to only a few with especially trained technicians. Could other tests more easily done substitute without any sacrifice? One which might possibly do so is the determination of sedimentation rates on the blood from the extremities. It would be well to have differential counts made on the same blood samples used for the platelet counts. In leukemia, purpura may not be present when high or not too extremely low platelet counts are present. This shows that there are other factors present determining bleeding when it does occur in leukemia, in addition to the mere number and quality of platelets. Dr. Maynard has charted a most interesting point to be used with other ones yet to be found to form a line pointing beyond academic interest to clinically useful information.

DR. MERLIN T. R. MAYNARD, San Jose, Calif: I thank Dr. Cornbleet for raising all these questions. I have thought of every one of them. Being a clinician, I hope that somebody with more laboratory time than I have will be able to dig into this side of it. I have always had the one technician do every count and she has been accurate. We can recheck the same individual over and over again and get the count within a very small margin of error. That has all been done on the laboratory side. Tourniquet tests? Yes, I would like to do them, and I would like to get some purpuras. I have done intracutaneous vitamin C tests, but they have not been very successful. The dye seems to be dispersed almost as rapidly in the pathologic areas as in the normal skin. I would like to see sedimentation rates done. The capillary microscope too. I did some of that work many years ago and I haven't thought of it in this case. We have done the differential counts and the interesting thing is that we get perfectly normal white cell and red cell counts, but the platelets are deficient. The platelets are the only ones that are severely interfered with in their distribution.

Skin Grafts.—The skin graft was first used in 1847 by the American surgeon F. H. Hamilton. In 1869, two years after he had demonstrated the parasitic properties of skin, Reverdin of Geneva introduced the so-called malpighian graft, 2 to 6 mm. in size. The technic of skin grafting was improved by Karl Thiersch of Munich, professor of surgery in Erlangen, who in 1874 described the method which has since been known by his name but with which Ollier's name should also be associated, for this great French orthopedic surgeon had already described a method exactly similar in 1872. The "pinch" graft, consisting of a small conical graft of skin about half a centimeter in diameter, is generally attributed to Staige Davis (1919). More recently the grafting of small pieces of skin was greatly improved by my own teacher Manuel Corachan, who in 1933 published an account of the technic with which he had obtained highly successful results. Since 1917 the chief exponent of the whole thickness living graft in the form of tubed pedicle flaps has been Sir Harold Gillies, to whose school the progress of modern plastic surgery has been so largely due.—Trueta, Joseph: The Principles and Practice of War Surgery, St. Louis, C. V. Mosby Company, 1943.

IRRADIATION OF THE SPLEEN AND PITUITARY FOR CONTROL OF PUBERAL BLEEDING

BIRTH OF A NORMAL CHILD FOLLOWING TREATMENT OF THE MOTHER

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An entirely unwarranted fear that irradiation may do harm to the generative organs is one of the main reasons why this well tested method is not more generally utilized in the treatment of irregular bleedings in young girls. While it is true, as Halberstaedter [1] reported early after the advent of x-rays, that these exercise a selective action on the ovaries, nevertheless, when roentgen therapy is properly employed, permanent suppression of ovarian function and damage rarely occur.

In 1939 I [2] reported the case of a young woman who, intensely irradiated over the pelvic area at 4 years of age, nonetheless menstruated at 12 years and now, at the age of 17½ years, continues to have regular periods. Commenting on this case, Dr. George L. Streeter [3] of the Carnegie Institute of Embryology states:

"I believe the factor involved in your case is the principle that the more primordial the cells the more resistant they are to x-rays, whereas ova in the later stages of their differentiation are easily destroyed by x-rays, and the primordial cells which will produce their successors are perhaps not so easily affected. In your case the heavy treatment that the patient received certainly killed off all the follicles but in the course of time the primordial ovarian tissue produced a new crop of eggs along with their accessory cells and this finally resulted in the resumption of menstruation."

It has been our experience [4] that the younger the woman treated for sterilization the less permanent is the menstrual suppression. It would appear as Streeter states that, while destruction of follicles does occur, primordial cells in the course of time develop new follicles and normal menstruation takes place. This evidently occurred in a case I [5] reported in 1930 in which, after a total sterilizing dose of x-rays, the patient resumed normal menstruation and subsequently gave birth to a normal child.

From my experience irradiation of young women and girls may be employed for gynecologic dyscrasias provided the dosage and method are properly selected. Not always is irradiation required directly over the ovaries. Béclère [6] was one of the first to demonstrate that irradiation of the pituitary may have an effect on menstruation. Since it has been established that the pituitary plays an important role in regulating the menstrual function under normal conditions, roentgen therapy has been applied to this area in an attempt to control menstrual disorders, thereby avoiding direct action on the ovaries. This method is especially effective in some cases of dysmenorrhea. In 1929 Ford and Drips [7] reported definite relief of menstrual irregulari-

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Read before the joint meeting of the Section on Obstetrics and Gynecology and the Section on Radiology at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 12, 1942.

1. Halberstaedter, L.: Berl. klin. Wchnschr. **42:** 64-66, 1905.
2. Kaplan, I. I.: Am. J. Obst. & Gynec. **37:** 158-160 (Jan.) 1939.
3. Streeter, George L.: Personal communication to the author in 1938.
4. Rubenfeld, Sidney, and Maggio, R. J.: Am. J. Obst. & Gynec. **26:** 237-243 (Aug.) 1933.
5. Kaplan, I. I.: Surg., Gynec. & Obst. **50:** 492-493 (Feb.) 1930.
6. Béclère, A.: Paris méd. **13:** 97, 1926.
7. Ford, F. A., and Drips, Della G.: Radiology **12:** 393-402 (May) 1929.

ties from roentgen irradiation of the pituitary along with irradiation of the spleen.

Definite information about the spleen function is still lacking, but, owing to the relationship between the spleen and the blood vascular system and thrombopenic purpura, splenic irradiation has been used for the control of various types of hemorrhages, especially those associated with ovarian or uterine origin. The effect is not entirely due to increasing coagulation nor does irradiation of the spleen produce a specific coagulation effect. Action through the lymphocytes is probable.

In 1923 Nurnberger [8] reported on the favorable results of irradiation to the spleen in internal hemorrhages and believed it due to the indirect effect on the ovaries and an increase of the blood coagulability. Borak [9] in 1924 recommended splenic irradiation for refractory gynecologic bleeding and suggested that the response was due to x-ray reaction on the nuclear substance, which produced a styptic effect. Seitz [10] reported the hemostatic effect of splenic irradiation in uterine bleeding. Martius [11] reported irradiation of the spleen not only effective in juvenile uterine hemorrhage but also effective in 75 per cent of the cases of bleeding due to ovarian conditions. Werner [12] found that hemorrhage at puberty was quite amenable to irradiation of the spleen and that 70 per cent of the cases responded to a single treatment. He believed that the effect was due to temporary disturbance of the control mechanism. He also noted the favorable effect of pituitary irradiation for such conditions.

Treatment over the spleen can be administered without much hazard of affecting the ovaries, the indirect effect on the ovaries being considerably less than the supposed damage resulting from direct ovarian irradiation in young women and girls. In menorrhagia at puberty or just beyond this period, roentgen therapy to the spleen and on the pituitary can be safely administered without interfering with subsequent ability to bear children.

The following case is an illustration of this sequence:

F. R. (now F. R. C.), a young Jewish girl aged 14½, was referred to me on Nov. 17, 1931 with a note from her physician stating that she started her menstrual history in January of that year. Her first two periods were characterized by slight staining and the last three or four periods were marked by profuse hemorrhages lasting for seven days or more followed by irregular staining.

She was kept in bed for several weeks and treated with various glandular medicaments without avail; also injections were given to raise the blood calcium, and as a last resort she was referred for roentgen therapy.

She was one of three children. The mother's menstrual history was normal. The patient as a child was frequently ill and at 4 suffered from chorea. She looked pale, although her blood examination showed only a mild anemia.

The patient was thin, pale and nervous. No vaginal examination was done. The abdomen was soft and no masses were felt. The spleen was not palpable. Rectally there was no pelvic abnormality discernible.

It was decided to institute roentgen treatments to forestall further bleeding. High voltage roentgen therapy was administered over the splenic area; the rest of the pelvis where the ovaries lay was not covered. The factors used were 180 kilovolts, 5 milliamperes, 0.5 mm. of copper and 2 mm. of aluminum filter, at 30 cm. distance through a 6 by 8 cm. port. An 18 per cent skin erythema dose was given (the roentgen measurement was not employed at that time).

On Dec. 11, 1931 she reported that menstruation had started on November 20, lasted but five days and was not so profuse as the previous one. Although she was requested to continue further treatments, the patient did not report again until Jan. 6, 1933, when she stated that, following the November 1931 menstruation, she did not bleed again for two months, after which menstruation was irregular until August 1932, when she bled for three weeks into September 1932. In October menstruation lasted four days. The following period was delayed till Dec. 25, 1932, when she started to bleed and was still bleeding profusely on Jan. 6, 1933, when she again reported to me for treatment. This was administered with a 20 per cent dose to the spleen and a 15 per cent dose to the pituitary area. I advised further treatment because it was felt that the single small dose would not be sufficient to give sustained control of the irregularity. However, the patient was not seen again until Sept. 20, 1933, when she reported having menstruated irregularly about every two months until September 5, when profuse bleeding started. She was treated with a 20 per cent dose of x-rays to the spleen and, as before, failed to return again until June 27, 1934, when she did so only because she had had continuous bleeding since June 17, 1934. A dose of 15 per cent roentgen therapy was given to the spleen and pituitary areas. Normal menstrual periods followed in July and August. On Nov. 2, 1934 severe bleeding started and on November 15 roentgen treatment was administered to the spleen (20 per cent dose) and to the pituitary (15 per cent dose). Normal menstruation followed until January 1935.

Severe bleeding appeared on Feb. 16, 1935. On March 13 a dose of 15 per cent was administered to the spleen and pituitary areas. Normal menstruation followed in April and May. In June there was no menstruation; on July 13 she began to bleed and continued until Aug. 2, 1935, when treatment was again given in 15 per cent doses to the spleen and pituitary areas. Bleeding lasted for ten days and then stopped. She then menstruated regularly for five to eight days until July 8, 1936, when bleeding was prolonged. On July 20, 1936 80 roentgens was given to the spleen. Regular periods followed until August 1937. On Aug. 10, 1937 70 roentgens was given to the spleen, with partial control of bleeding. On August 28 sudden hemorrhage occurred and continued until Sept. 21, 1937, when treatment was given to the spleen and pituitary areas, a dose of 150 roentgens and 75 roentgens administered to each area respectively. Bleeding stopped the next day.

Following this last treatment normal menstruation was established lasting two to three days and continued regularly thereafter. In September 1939, at the age of 22, she married and regular menstruation continued. In May 27, 1941 she reported having skipped two menstrual periods and examination revealed a pregnancy. She carried this normally and on Feb. 6, 1942 was delivered of a normal, full term baby girl.

COMMENT

Since x-rays are known to have a selective action on the ovaries, the use of this modality in the treatment for irregular bleeding in young girls has been deemed inadvisable and other areas to be irradiated were sought for controlling puberal bleeding. However, even though in some instances radiation must be administered directly to the ovaries, seldom is sterilization in young women permanent, and whereas ova in the later stages of their differentiation are readily destroyed by irradiation, the primordial cells which will produce subsequent ova are not affected. The ova will develop later and, when impregnated, produce normal children.

Because of the recognized controlling influence of the spleen in hemorrhage, roentgen therapy to the spleen has been employed with good results in gynecologic bleedings. The pituitary too is definitely related to the reproductive organs and has been shown to have a pronounced influence on menstrual function. Irradiation of the pituitary has been found to affect favorably gynecologic dyscrasias. Treatment of the spleen and pituitary offers a readily available and effective method

8. Nurnberger, L.: Zentralbl. f. Gynec., Jan. 6, 1923; abstr. Am. J. Roentgenol. **10:** 931 (Nov.) 1923.
9. Borak, J.: München. med. Wchnschr. **71:** 1119-1121 (Aug. 15) 1924.
10. Seitz, L.: Strahlentherapie **24:** 227-252, 1926.
11. Martius, H.: Strahlentherapie **21:** 242-259, 1926.
12. Werner, P.: Am. J. Obst. & Gynec. **13:** 54-60 (Jan.) 1927.

for treating puberal bleeding without direct irradiation of the ovaries, thus removing any fear of possibly adverse effect on the result of future pregnancy.

SUMMARY

A young woman, suffering from irregular menstrual bleeding and hemorrhage for nine years, previously having been treated with medication without response, was moderately controlled by roentgen therapy to the spleen and pituitary and eventually resumed normal menstruation. She married at 22½ years and gave birth to a perfectly normal child about two years later. Roentgen therapy, while controlling the uterine bleeding, has no injurious effect on the reproductive organs of the mother or on the child.

While I have treated a considerable number of girls for puberal bleeding, this case has been singled out for a detailed report because it is the first in the series in which the patient has married and borne children, thereby substantiating the repeatedly voiced opinion that roentgen therapy when properly administered will control abnormal puberal bleeding and leave no injurious effect either on the reproductive organs of the mother or on her children.

755 Park Avenue.

ABSTRACT OF DISCUSSION

Dr. Richard W. TeLinde, Baltimore: In the last five years in no instance have I used irradiation for the treatment of functional bleeding in women under 35 years of age. I believe it practically never is necessary and the likelihood of the menopause cannot be predicted with certainty. Women are variable in their susceptibility and even with carefully regulated small doses intended to produce temporary amenorrhea I have seen some very tragic permanent amenorrheas in young women irradiated by excellent radiologists. I can't agree with Dr. Kaplan when he speaks of supposed damage of x-rays to the ovary. It is not a supposition; it is real. We can see the histologic changes under the microscope and we can follow our cases clinically and see amenorrhea of varying lengths of time with distressing menopausal symptoms.

Dr. John T. Murphy, Toledo, Ohio: With regard to the pituitary irradiation of Dr. Kaplan, my experience has been that we are able, at least in the majority of cases, at the first treatment to control for varying periods of time the menstrual cycle. However, I have also had the experience of recurrent bleeding in which irradiation was not effective. There again it may be that we don't know the proper dosage to use, and I feel that that may be an answer to that.

Dr. Willard M. Allen, St. Louis: I have been much interested in Dr. Kaplan's results from irradiation of the pituitary. He had recurrences in his patients the same as in these cases which I have followed. This indicates a fundamental defect in these particular patients in the pituitary relationship.

Dr. Ira I. Kaplan, New York: The question of the advantage and disadvantage of treating young women with x-rays has been gone over completely during the last number of years, and we haven't made any definite decision as to what was what. As yet nobody has been able to produce for observation the second or third generation of human beings from people with hormone dyscrasias who have been irradiated. I have a large series of amenorrhea and sterility cases and a large number of children who have been born from these women who have been stimulated, as we call it, by x-rays to the ovary and the pituitary. We are not sure what the pituitary function is. We know it has a definite relation to ovarian function or menstrual function, or even the birth function in the female. It is too soon to state definitely what the after generation of human beings will show, but we can say that so far none of these children show abnormal effects. The oldest child is a boy normally well developed. Boys don't marry as young as girls, so we can't tell much about them except from the anatomic standpoint. The oldest girl I have in my series is now about 15. She is menstruating normally. I have a group of them now that are commencing menstruation, and they are menstruating normally. This is the first generation of the irradiated mother. I can show a girl who at 4½ had a sarcoma of the pelvis, who was one of the fortunate ones that survived. She had intensive irradiation with complete disregard of any ovarian protection. It was to save her life and keep her going because the parents wanted her to live. She had radium and x-rays. She had radium in the rectum; she had x-rays through the pelvis, two intensive courses, enough to warrant a first degree burn of the skin. Now at 17½ she is menstruating normally. One thing about our work in radiation has been left out in all these discussions. No gynecologist ever sends a patient to a radiation therapist unless he has exhausted everything else in the way of treatment, and so in every one of the cases that we have reported treatment has been administered by everything else that is known. Irradiation, properly given, should not be looked on as a death dealing ray, as something one should avoid.

Dr. Conrad G. Collins, New Orleans: It is gratifying to find that in relatively few cases, let's say, of puberty or puberal bleeding do we need to use surgery or irradiation, and it can be adequately controlled by endocrine measures in a large number of cases; but perhaps some of the gains made in that area have been lost at the menopause when too much endocrine therapy has been used in an attempt to control bleeding where it may do good temporarily but where the diagnosis is not made correctly, where a few cases of carcinoma are overlooked, where the results are not permanent, and here at this age of life surgery primarily, irradiation secondly, are indicated.

THE DURATION OF PASSIVE TETANUS IMMUNITY

AND ITS EFFECT ON ACTIVE IMMUNIZATION WITH TETANUS TOXOID

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ST. LOUIS
AND
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In the treatment and prophylaxis of tetanus there are several questions of considerable clinical importance for which there are insufficient data to warrant definite answers. Among these may be mentioned:

1. What is the duration of antitoxic immunity after the usual therapeutic dose of tetanus antitoxin?
2. Does any stimulation of antitoxin accompany an attack of clinical tetanus?
3. Can an active antitoxic immunity against tetanus be produced by repeated subcutaneous or intracutaneous injections of toxoid with sufficient rapidity so that such a method could be used as a prophylaxis for wounds?
4. Does the presence of heterologous antitoxin from passive immunization interfere with active immunization against tetanus by toxoid?
5. Has Ramon's "simultaneous serovaccination" against tetanus any merit?

In this paper we wish to report observations on the immunization of children with clinical tetanus and of normal children which give information on these questions.

MATERIAL AND METHODS

The observations here reported include more than four hundred tetanus antitoxin titrations made on 9 children with clinical tetanus treated in the St. Louis

From the Department of Pediatrics, Washington University School of Medicine, the St. Louis Children's Hospital, and the Shriner's Hospital for Crippled Children, St. Louis, and the Lilly Research Laboratories, Indianapolis.

Children's Hospital and on 30 children, aged 8 to 15 years, in the Shriner's Hospital for Crippled Children who were in good health and under orthopedic treatment for various deformities. Permission to carry out experimental tetanus immunizations on the latter was given by the chief of staff, Dr. C. H. Crego. The antitoxin determinations were done under the direction of one of us (F. G. J.) and expressed as American units. The titers given represent minimal values in units per cubic centimeter, since the titrations were done at the following levels: 50, 30, 20, 10, 7.5, 5, 2, 1, 0.5, 0.2, 0.1, 0.05, 0.02, 0.017, 0.01 and 0.003 units. A reading of 0.2 would mean, for example, more than 0.2 unit and less than 0.5 unit. Less than 0.003 unit is tabulated as 0.

In the first series of experimental immunizations (table 3) in which toxoid was injected subcutaneously and intracutaneously, plain (fluid) rather than alum precipitated toxoid was used, since it was considered that a more rapid absorption of the antigen might make the observations more definite than the prolonged and lingering action of the insoluble alum precipitated toxoid. The intracutaneous injection of 0.5 cc. produced no special discomfort.

In the later series on experimental "simultaneous" and delayed immunization (table 4) with toxoid, the insoluble alum precipitated form was used because it was considered desirable to have a more prolonged and continuous action.

For simplicity in presentation, the results will be given in tabular form, and condensed protocols of the observations on the patients with tetanus will be appended at the end of the paper.

THE DURATION OF PASSIVE ANTITOXIC IMMUNITY

Passive immunization with tetanus antitoxin is generally believed to be of short duration. For example, in standard works on immunology Zinsser [1] states "In ordinary human cases, the antitoxin injected into man may be expected to disappear from the circulation within about three weeks," and Topley and Wilson,[2] "Passive immunity conferred by a single injection of (tetanus) antitoxin wears off in about a fortnight or three weeks." In support of such statements are quoted the observations of Glenny and Hopkins,[3] in which 3 rabbits were given 0.5 cc. (375 units) of diphtheria antitoxin and an initial value of 6 to 11 units of antitoxin per cubic centimeter in the blood was reduced to 0 in eleven to sixteen days, and of Smith,[4] who reported that after the subcutaneous injection of 9,000 units of diphtheria antitoxin a man showed 1.13 units on the 4th day, 0.08 unit on the 20th day and none on the 27th day after the injection. From clinical observation also it has been noted that diphtheria or tetanus may occasionally develop two to three weeks after a prophylactic antitoxin injection of 500 to 1,500 units has been given. Recently Bigler and Werner [5] carried out antitoxin titrations on the blood of 64 children aged 3 to 10 years at varying times after the injection of 1,500 units of tetanus antitoxin. They found a wide variation in antitoxin titers in different children and found that some responded less well than others. During the 3d week the tendency was for the level to fall to 0.01 unit, although some remained as high as 0.1 unit and others fell to 0.003 unit or less. In those cases in which there is a more rapid disappearance of passive immunity, the possibility of a previous injection of serum should be kept in mind, since under such circumstances the injected serum is destroyed more quickly, as shown by Sacquépée and Jude,[6] who made a similar study on adults after passive prophylaxis with 3,000 (international) units of tetanus antitoxin. There seems little question that with such relatively small doses of antitoxin passive immunity is of short duration. On the other hand, when larger doses of antitoxin are given, there is evidence that, although the early high titers fall within a short period, lower levels of antitoxin may persist in the blood for a much longer time.

Actual titrations of antitoxin levels in man after passive tetanus immunization with large doses of antitoxin in clinical tetanus are relatively few, although Dean [7] demonstrated tetanus antitoxin (amount not stated) twenty, thirty and thirty-nine days after the intravenous injection of 30,000 units, and Cole and Spooner [8] made observations on 4 patients each given 200,000 units of tetanus antitoxin and in all instances found 10 units after seven days, 3 to 5 units after fourteen days and in 3 cases 1 to 3 units after one month, while the fourth patient had 0.33 unit on the 22d day and more than 0.1 unit on the 41st and 63d day. Ramon and his associates [9] have reported antitoxin titers on 2 adults each given 150,000 (international) units of tetanus antitoxin. (The international unit is half the strength of the American unit.) In 1 of these a titer of 0.1 unit was found on the 49th day and 0.03 unit on the 70th day, while in the other at least 0.1 unit persisted for thirty-seven days and 0.03 unit for forty-nine days. Two other adults who had had serum injections some time previously were also observed after the injection of 150,000 units of tetanus antitoxin. In these the antitoxin disappeared much more rapidly and 0.01 to 0.1 unit persisted for only twenty-eight days. The more rapid disappearance of antitoxin in animals and persons who have had previous serum injections is the rule and to be expected. Sohier and Jude [10] followed the antitoxin in a patient who received 1,254,000 units of tetanus antitoxin over a period of eleven days and reported 1 unit present after thirty-nine days, and 0.01 unit was found on the 86th and again on the 106th day after the last antitoxin injection.

The actual level of antitoxin in the blood required to produce clinical immunity to tetanus has not been definitely established, but there is conclusive evidence that higher values are necessary in passively immunized animals than in those actively immunized. The evidence for this conclusion from animal experiments will

1. Zinsser, Hans, and Bayne-Jones, Stanhope: Textbook of Bacteriology, ed. 8, New York and London, D. Appleton-Century Company, 1939, p. 163.
2. Topley, W. W. C., and Wilson, G. S.: The Principles of Bacteriology and Immunity, ed. 2, Baltimore, William Wood & Company, 1937, p. 1367.
3. Glenny, A. T., and Hopkins, B. E.: Duration of Passive Immunity, J. Hyg. **21**: 142 (Nov.) 1922.
4. Smith, J. H.: On the Absorption of Antibodies from the Subcutaneous Tissues and Peritoneal Cavity, J. Hyg. **7**: 205 (April) 1907.
5. Bigler, J. A., and Werner, Marie: Active Immunization Against Tetanus in Infants and Children, J. A. M. A. **116**: 2355 (May 24) 1941.
6. Sacquépée, E., and Jude, A.: Sur l'immunité conférée par le sérum antitétanique, Rev. d'immunol. **3**: 444 (Sept.) 1937.
7. Dean, R. H.: Report on Twenty-Five Cases of Tetanus to the Medical Research Committee, Lancet **1**: 673 (May 5) 1917.
8. Cole, Leslie, and Spooner, E. T. C.: The Treatment of Tetanus with Observations on the Fate of Injected Antitoxin, Quart. J. Med. **4**: 295 (July) 1935.
9. Ramon, Gaston; Kourilsky, Raoul; Richou, R., and Kourilsky, Simone: Recherches immunologique sur la séro-anatoxithérapie tétanique, Rev. d'immunol. **5**: 432 (Sept.) 1939.
10. Sohier, R., and Jude, A.: Recherches sur le sort de l'antitoxine chez un tétanique traité par la sérothérapie spécifique associée à l'anesthésie générale, Bull. et mém. Soc. méd. d. hôp. de Paris **1**: 80 (Jan. 14) 1938.

be published in detail by one of us (F. G. J.) in a future paper. From our present knowledge it would appear a valid assumption that in human beings clinical protection from tetanus requires a titer of 0.01 to 0.1 unit of passively introduced antitoxin while an active immunity of 0.001 to 0.01 unit is sufficient.

PASSIVE IMMUNITY AFTER LARGE DOSES OF ANTITOXIN

In table 1 are shown tetanus antitoxin titrations on 8 children who were given 100,000 units or more in the treatment of clinical tetanus and in whom the rate of disappearance of the passive immunity was followed for a number of weeks. With these larger doses there was remarkable constancy in the rate of decrease in antitoxin, although in those given more than 100,000 units (cases 1 and 2) there was a higher early level and a somewhat longer persistence of the passive immunity. It will be noted that, while the high initial titers fall quickly, as much as 1 unit remained from three to four weeks after the injection, 0.1 unit from six to ten weeks and 0.01 unit from eight to eleven weeks. In the single observation after 150,000 units was given, the antitoxin persisted longer than in the others after 100,000 units. In case 2 also the concentration of antitoxin in the spinal fluid was determined on two occasions. On the 3d day the blood showed 50 units, and on the 9th day the blood titer was 30 units, and on both these occasions the spinal fluid had a titer of 0.2 unit per cubic centimeter. Another patient (case 7) had only 0.017 unit in the spinal fluid when the blood titer was 70 units.

When only moderately large doses of antitoxin were given (10,000 units) the duration of a more prolonged passive immunity was somewhat less constant than after 100,000 units or more. In table 2 are collected observations on 21 children after receiving 10,000 units, and the duration of titers as high as 0.1 unit and 0.01 unit is shown. These are summarized from data in tables 3 and 4, which will be mentioned later. It will be noted that in 14 of the 21 children a titer of 0.1 unit persisted for from four to six weeks and a titer of 0.01 unit from six to ten weeks. None of these had had a previous serum injection, while of the 7 subjects whose antitoxin disappeared more rapidly only 2 had had horse serum previously. One other child, a girl aged 14 years, was of special interest, since she showed less than 0.003 unit when tested only two weeks after receiving 10,000 units intramuscularly. Careful inquiry elicited no history of a previous serum injection.

To summarize these observations, it was found that after the injection of 10,000 to 150,000 units the tendency is for tetanus antitoxin to persist in the blood in a titer of 0.1 unit for four to eight weeks, and 0.01 unit remains for eight to ten weeks. It was observed in 1 case also that even with a blood antitoxin titer of 30 to 50 units the spinal fluid contained only 0.2 unit, and another patient showed 0.017 unit in the spinal fluid at a time when the blood contained 70 units. In this connection it is of interest that Sohier and Jude [10] found only 0.03 to 0.1 unit per cubic centimeter in the spinal fluid of their patient at a time that the blood showed 50 to 100 (international) units, in spite of the fact that 50,000 units had been injected intrathecally sixteen hours previously.

THE ABSENCE OF ANY ANTITOXIN STIMULATION BY AN ATTACK OF CLINICAL TETANUS

It has long been recognized that tetanus infection does not produce a permanent antitoxic immunity, since a demonstrable antitoxin does not persist in the blood after recovery. The usual explanation is that tetanus toxin is so potent that the absorption of an amount sufficient to produce clinical symptoms is too minute a quantity of antigen to stimulate the production of antitoxin. However, it might be possible for sufficient antigen to be absorbed to produce a primary antigenic stimulus such as occurs after an initial dose of toxoid and which sensitizes the cells to a later, more effective secondary stimulus. This could be determined by a toxoid injection after recovery from tetanus. In all, we have made observations on 4 children with clinical tetanus, and none showed any development of tetanus antitoxin when toxoid was given some time after recovery. Two of these (table 1, cases 2 and 3) already mentioned received toxoid injections during the first week of observation, and neither responded by a rapid development of antitoxin when given a stimulating dose of toxoid two and one-half to three and one-half months later. A third (case 4) had 100,000 units of tetanus antitoxin, all of which had disappeared from the blood in four months, at which time a subcutaneous injection of 1 cc. of toxoid was given, but no antitoxin had developed two months later. One child (case 5) had typical but mild tetanus of two weeks' duration when first seen. He was given no antitoxin and recovered within two weeks, without

TABLE 1.—*Serum Tetanus Antitoxin Titrations in American Units in Eight Children After Passive Immunization with 100,000 Units or More*

Case	Age, Yr.	Units of Antitoxin Given	Day After Antitoxin Injection																				
			1	3	4	7	9	12	14	17	21	24	28	32	35	37	42	47	49	57	63	68	76	80
1. Ruby C.....	5	200,000	..	..	..	..	..	20	..	10	..	..	..	..	..	..	..	..	..	..	..	..	..	..
2. Noreen B....	8	150,000	..	50	..	..	30	20	..	10	..	..	0.5	..	..	..	..	..	..	..	..	0.1	..	0.01
3. Ruth R.....	10	100,000	..	20	..	..	10	7.5	5	..	..	2	..	1.0	..	0.5	..	0.2	..	0.1	..	..	0.01	..
4. Clement H..	13	100,000	..	..	20	..	10	..	5	..	..	..	0.5	..	..	..	0.1	..	..	0.01	..	..	..	..
5. Charles K...	13	100,000	..	30	..	..	..	..	..	2	..	1	..	..	..	..	..	..	..	..	..	..	..	..
6. Geneva G...	3	100,000	..	..	..	20	..	..	5	..	2	..	1	..	0.2	..	0.2	..	0.1	..	..	..	..	..
7. Raymond N.	7	100,000	70	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
8. Mary W.....	6	100,000	..	..	40	..	10	..	5	..	2	..	1	..	0.5	..	0.2	..	0.1	..	0.017	..	..	..

TABLE 2.—*Duration of Titers of 0.1 and 0.01 Unit of Tetanus Antitoxin in the Serum of Twenty-One Children After the Injection of 10,000 Units Intramuscularly*

	Weeks After Administration								
	<2	2	3	4	5	6	8	9	10
Number with 0.1 unit....	1	6	..	9	1	4	..	..	..
Number with 0.01 unit...	1	..	1	5	..	3	5	2	4

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the developing of any demonstrable antitoxin in the blood. About seven weeks after the first symptoms, a subcutaneous injection of 1 cc. of toxoid was given, but no antitoxin developed during the following nine weeks.

These observations confirm the prevailing belief that immunity to tetanus does not follow an attack of the disease and in addition indicate that the amount of tetanus toxin antigen absorbed is so small as to produce no primary stimulus or sensitization to tetanus immunization.

THE POSSIBILITY OF RAPID DEVELOPMENT OF ACTIVE TETANUS IMMUNITY FOR PROPHYLAXIS

The use of toxoid immunization for prophylaxis after wounds has never been seriously considered by immunologists as a substitute for passive immunization with antitoxin, because the time required for the development of active immunity is considerably longer than the incubation period of tetanus. However, the question is sometimes raised by clinicians whether by repeated intracutaneous toxoid immunization a more rapid production of antitoxin could be stimulated. In the group of 4 children (group 3, table 3) observed after the intradermal injection of 1 cc. of tetanus toxoid every 2d day until four doses had been given it was found that the blood titer of antitoxin remained below 0.003 unit for the following seven weeks. Another group (group 1, table 3) immunized by subcutaneous injection of toxoid showed a similar lack of antitoxin production. There is no evidence from these observations that either repeated subcutaneous or intracutaneous injections of tetanus toxoid stimulate a more rapid development of antitoxin.

THE EFFECT OF PASSIVE IMMUNITY ON ACTIVE IMMUNIZATION WITH TETANUS TOXOID

The early observations of Glenny and Südmerson [11] on immunization of guinea pigs against diphtheria with toxin or toxin-antitoxin showed that an animal slightly immunized by a previous dose of antigen responds promptly to a second later injection by a rapid production of antitoxin, but if passively immunized with antitoxin when the first antigen was given a later antigen injection stimulates no secondary type of response and in fact no antitoxin may be produced at all. This principle of the inhibition of active immunization by the presence of passive immunity has been rather generally accepted, and it is only in recent years that reports, chiefly by Ramon [12] and his associates, have advocated combining active and passive immunization by the simultaneous injection of antitoxin and toxoid in diphtheria and tetanus. This consists of an initial injection of antitoxin and one of toxoid followed after an interval by a second toxoid injection and preferably later a third dose of toxoid.

The previous work along this line, especially with diphtheria, has been summarized and reviewed in a recent paper by Downie and his associates,[13] who made an extensive series of observations on the combined active and passive immunization of 300 young adults against diphtheria. They conclude from the papers reviewed and from their own work that the simultaneous administration of antitoxic serum with the first dose of toxoid interferes somewhat with the primary response of the tissues but does not destroy it. Although there may be some delay and slight degree of inhibition in the formation of antitoxin, the final degree of immunity following a later dose of toxoid does not appear to be much inferior to that resulting from active immunization alone. A similar interference with the development of active immunity against tetanus by antitoxin was found by Otten and Hennemann.[14]

Many workers have concluded that only free toxoid can produce the primary sensitization of tissues for an active immunity response to a later injection and that if an excess of antitoxin is present the neutralized toxoid has little sensitizing effect. In this connection two considerations are of some importance: (1) the fact that small doses of antitoxin persist in the body for a much shorter time than large doses, as discussed previously, and (2) the fact that, although plain (fluid) toxoid when injected is either immediately neutralized by any antitoxin present or combines rapidly with tissue cells to sensitize them, alum precipitated toxoid is insoluble and remains for some days or weeks at the site of injection and only as the insoluble precipitate goes slowly into solution does the toxoid gradually become available either for neutralizing antitoxin or for sensitizing tissues. In almost all the experimental observations the dose of antitoxin has been 1,500 units or less, and in some of them, especially the later ones, alum precipitated toxoid has been used. It is apparent that the inhibiting effect of antitoxin on the sensitizing action of early injections of toxoid might be more certainly observed by the use of a moderately large dose of antitoxin and plain toxoid, since alum precipitated toxin presumably has a more continuous and prolonged absorption.

Our first observations on combined immunization were carried out on 18 healthy children and are summarized in table 3, in which is shown a comparison of the effect of toxoid alone with serovaccination by making weekly titrations of tetanus antitoxin in the blood.

In group 1 each of 4 children received 1 cc. of plain (fluid) tetanus toxoid subcutaneously every 2d day until four doses had been given, and eight weeks later a single subcutaneous dose of 1 cc. of toxoid. As will be noted, no tetanus antitoxin was detectable in the blood following the first series of injections but appeared quickly after the stimulating dose given eight weeks later.

In group 2 the same procedure was followed except that each of the 4 children received 10,000 units of tetanus antitoxin on the first day on which toxoid was given. There was a progressive decrease in (passive) antitoxin titer, and in 1 child (case 3) who had had a previous serum injection the antitoxin had disappeared entirely at the end of five weeks. In none did the toxoid given after eight weeks stimulate the production of any antitoxin within a period of two weeks.

Groups 3 and 4 were identical with groups 1 and 2 except that in them the initial series of toxoid injections was given intracutaneously. The results were the same in that no antitoxin appeared after the later

11. Glenny, A. T., and Südmerson, H. J.: Notes on the Production of Immunity to Diphtheria Toxin, J. Hyg. **20**: 176 (Oct.) 1921.

12. Ramon, Gaston: Combined (Active-Passive) Prophylaxis and Treatment of Diphtheria or Tetanus, J. A. M. A. **114**: 2366 (June 15) 1940.

13. Downie, A. W.; Glenny, A. T.; Parish, H. J.; Smith, W., and Wilson, G. S.: Combined Active and Passive Immunization Against Diphtheria, Brit. M. J. **2**: 4220 (Nov. 22) 1941.

14. Otten, L., and Hennemann, I. P.: Combined (Simultaneous) Immunization Against Tetanus, Mededeel v. d. dienst d. volksgezondh. in Nederl.-Indië **28**: 283, 1939; abstr. J. A. M. A. **114**: 1028 (March 16) 1940.

stimulating dose of toxoid in the children who had received a dose of antitoxin at the outset, although those to whom antitoxin had not been given responded promptly in the usual manner by the development of an active immunity.

The results of these experiments were clearcut and definite. They show that the presence of any considerable quantity of injected antitoxin prevented the primary sensitization or "primary response" of the body cells by doses of toxoid injected during the 1st week, so that a later single dose of toxoid was ineffective in stimulating active antitoxin production.

Further observations on the inhibiting effect of antitoxin on immunization by alum precipitated tetanus toxoid were made on 2 children with clinical tetanus treated with antitoxin and given toxoid simultaneously. Brief protocols of these 2 cases (2 and 3) are given later.

The second child (case 3), a girl aged 10 years, was given 50,000 units of tetanus antitoxin on the first day of observation and the same amount on the following day. Alum precipitated tetanus toxoid (0.5 cc.) was given intracutaneously on the first day and on each of the following six days. In table 1 are given the blood antitoxin titers, which fell to 0.017 unit on the 76th day. On the 111th day less than 0.003 unit was found, and at this time 1 cc. of alum precipitated tetanus toxoid was given subcutaneously. One week later the blood still showed no antitoxin, although four weeks after the toxoid injection (141st day) the serum titer was 0.2 unit, which had decreased to 0.05 unit after five and one-half months. At this time a final dose of 1 cc. of plain tetanus toxoid subcutaneously was followed by a titer of 2 units after one week and 5 units after two weeks. In this case the early injections of toxoid apparently produced no primary sensitization, since a

TABLE 3.—*Comparison of Tetanus Toxoid Immunization Alone and "Serovaccination," Both Subcutaneous and Intracutaneous Injections Being Used*

		Blood Tetanus Antitoxin Titrations in Units														
Day of observation.....		1	2	3	5	7	8	15	22	28	35	42	49	56	63	70
	Group 1															
1	Boy 9 yrs.	0*	...	*	*	*	0	0	0	0	0	0	0	0*	0.05	0.1
2	Boy 11 yrs.	0*	...	*	*	*	0	0	0	0	0	0	0	0*	0.1	0.2
3	Girl 9 yrs.	0*	...	*	*	*	0	0	0	0	0	0	0	0*	0.1	0.2
4	Girl 14 yrs.	0*	...	*	*	*	0	0	0	0	0	0	0	0*	0.017	0.1
	Group 2 †															
1	Girl 9 yrs.	0*	2.0	*	*	*	1.0	0.5	0.2	0.2	0.1	0.1	0.05	0.05*	0.05	0.017
2	Girl 11 yrs.	0*	1.0	*	*	*	1.0	0.1								
3	Boy 13 yrs.	0*	2.0	*	*	*	0.5	0.2	0.05	0.017	0	0	0	0*	0	0
4	Boy 15 yrs.	0*	0.5	*	*	*	1.0	0.2	0.1	0.1	0.05	0.017	0.017	0.017*	0.01	0.003
	Group 3															
1	Girl 11 yrs.	0‡	...	‡	‡	‡	0	0	0	0	0	0	0	0*	0.05	0.2
2	Girl 13 yrs.	0‡	...	‡	‡	‡	0	0	0	0	0	0	0	0*	0.1	0.5
3	Boy 11 yrs.	0‡	...	‡	‡	‡	0	0	0	0	0	0	0	0*	0.1	0.2
4	Boy 10 yrs.	0‡	...	‡	‡	‡	0	0	0	0	0	0	0	0*	0	0.017
	Group 4 †															
1	Girl 12 yrs.	0†	1.0	‡	‡	‡	2.0	0.5	0.2	0.1	0.05	0.05	0.017	0.017*	0.003	0
2	Girl 10 yrs.	0†	5.0	‡	‡	‡	2.0	0.5	0.2	0.2	0.1	0.05	0.05	0.05*	0.017	0.017
3	Boy 9 yrs.	0†	2.0	‡	‡	‡	2.0	0.5	0.2	0.2	0.1	0.1	0.05	0.05*	0.017	0.017
4	Boy 13 yrs.	0†	1.0	‡	‡	‡	0.5	0.1	0.017	0	0	0	0	0*	0	0
	Group 5 † (control)															
1	Boy 14 yrs.	0	1.0	..	..	..	1.0	0.5	0.2	0.1	0.05	0.017	0.017	0.017*	0.003	0
2	Boy 12 yrs.	0	2.0	..	..	..	1.0	0.2	0.1	0.1	0.05	0.05	0.017	0.017*	0.01	0.003

* 1 cc. of fluid tetanus toxoid subcutaneously. † 10,000 units of tetanus antitoxin intramuscularly.
‡ 1 cc. of fluid tetanus toxoid intracutaneously (2 areas 0.5 cc. each).

The first child (case 2), a girl aged 8 years, was given 100,000 units of tetanus antitoxin the first day of observation and 50,000 units two days later. Alum precipitated tetanus toxoid (0.5 cc.) was injected subcutaneously the first day and on each of the succeeding six days. Determinations of tetanus antitoxin in the blood (table 1) showed a decreasing titer, until on the 68th day 0.1 unit was present. Six days later (74th day) 1 cc. of alum precipitated toxoid was given subcutaneously, but the antitoxin continued to fall to 0.017 unit on the 80th day and to 0.003 unit on the 125th day. This indicated that the sensitizing effect of early doses of alum precipitated toxoid had been prevented by antitoxin. On the 125th day 0.5 cc. of alum precipitated tetanus toxoid was given subcutaneously with the development of 0.5 unit antitoxin two months later (177th day), at which time an additional subcutaneous injection of 0.5 cc. of alum precipitated toxoid resulted in an antitoxin titer of 5 units two weeks later (185th day).

stimulating dose of toxoid three and one-half months later resulted only in the type of response often seen from the first antigen injection. The rapid stimulation of the typical "secondary" response followed a later dose of toxoid.

The observations on these 2 children show that the presence of heterologous tetanus antitoxin inhibited the sensitizing effect of alum precipitated tetanus toxoid given subcutaneously or intracutaneously daily during the first week of such passive immunity, so that a later injection of toxoid did not stimulate antitoxin formation in the prompt manner to be expected from a secondary response.

DEVELOPMENT OF ACTIVE IMMUNITY IN PASSIVELY IMMUNIZED PERSONS

In spite of the inhibition of (passive) antitoxin immunity on the sensitizing effect of early administration of toxoid, it is apparently possible to overcome this inhibition by repeated toxoid injections so that

a state of passive immunization can pass into one of active immunity. This appears to be more readily accomplished when small amounts of antitoxin are given than after large doses. Sacquépée and Jude,[15] for example, treated 240 wounded soldiers prophylactically for tetanus by giving 1.5 cc. of anatoxin (toxoid) subcutaneously together with "the dose of serum indicated by the circumstances." On the 20th day and again on the 30th day, 2 cc. of toxoid was given subcutaneously. Antitoxin titrations done six months later showed that 97 per cent of the subjects had 0.065 to 0.2 (international) unit of tetanus antitoxin. After one year an additional dose of 2 cc. of toxoid was given and six months later, when 51 were retested, 96 per cent had more than ⅓ unit and 76 per cent 1 unit or more.

TABLE 4.—*Combined Passive and Active Tetanus Immunization: Comparison of "Simultaneous Serovaccination" with Delayed Toxoid Injections After 10,000 Units of Antitoxin in the Production of Active Immunity*

Elapsed week of observation.....	Blood Tetanus Antitoxin Titration in Units						
	0	2	4	6	8	10	12
Group 1 *	†	†	†	†	†	†	
1. Girl 13 yrs.	0	1.0	0.2	0.1	0.05	0.017	**0.1**
2. Girl 10 yrs.	0	0.5	0.05	0.003	0	**0.2**	0.2
3. Boy 14 yrs.	0	0.2	0.05	0.017	**0.1**	0.5	0.5
Group 2 *		†	†	†	†	†	
1. Girl 12 yrs.	0	0.5	0.05	0	**0.2**	0.5	1.0
2. Girl 13 yrs.	0	0.2	0.1	0.017	0.01	**0.2**	0.5
3. Boy 9 yrs.	0	0.2	0.01	0	**0.2**	0.5	2.0
Group 3 *			†	†	†	†	
1. Girl 12 yrs.	0	0	0	0	0	**0.1**	0.2
2. Girl 14 yrs.	0	0.5	0.2	0.003	0	**0.1**	0.2
3. Boy 9 yrs.	0	1.0	0.2	0.1	0.05	0.05	**1.0**
Group 4 *				†	†	†	
1. Girl 10 yrs.	0	1.0	0.1	0.017	0.003	0	**0.2**
2. Girl 14 yrs.	0	0.5	0.1	0.017	0.003	0	**0.2**
3. Girl 8 yrs.	0	1.0	0.2	0.05	0.017	**0.1**	1.0
Group 5 ‡		†	†	†	†	†	
1. Girl 14 yrs.	0	0.017	0	**0.1**	0.2	0.5	0.5
2. Girl 13 yrs.	0	0.017	0	**0.003**	0.2	0.2	0.5
3. Boy 15 yrs.	0	0.1	0.017	0	**0.003**	0.2	0.2

* 10,000 units of tetanus antitoxin intramuscularly.
† 0.5 cc. of tetanus toxoid (alum precipitated) subcutaneously.
‡ 1,500 units of tetanus antitoxin intramuscularly.

When larger (therapeutic) doses of antitoxin are given together with toxoid, the development of demonstrable active immunity may require a prolonged period of repeated antigen injections and the lapse of several months. The observations by Ramon,[9] who has advocated this procedure of simultaneous immunization, are the only ones reported in sufficient detail to be of value for analysis. This report comprises 14 patients each of whom received 150,000 (international) units of tetanus antitoxin together with 2 cc. of anatoxin (toxoid). At weekly intervals increasing doses of toxoid were given (3 cc. in one week, 4 cc. in two weeks, 5 cc. in three weeks, 5 cc. in four to seven weeks and sometimes 5 cc. later) and titrations of tetanus antitoxin followed. The early high antitoxin titers fell rapidly to lower levels, and the later decrease in titer was more gradual. In every instance there was eventually an increase in antitoxin as evidence of the production of an active immunity which appeared two weeks after a toxoid injection. Most cases, however, required a total of six injections of toxoid (24 to 29 cc.) and the development of active immunity was not demonstrated for four months or more (seventeen weeks 2, nineteen weeks 3, twenty-three weeks or more 4), although 3 patients showed some increase in antitoxin at the end of eight weeks and 2 others at ten weeks. It was of interest also that in most instances the (passive) antitoxin had fallen to a relatively low level before a stimulating dose of toxoid caused a rise in titer. For example, in 5 cases the titer had reached less than 0.01 unit, while in 7 others it had fallen to 0.1 unit or less. It was assumed by Ramon that the early "simultaneous" dose of toxoid was necessary or at least played a very important part in the sensitization. It may be pointed out, however, that the evidence previously mentioned of the inhibiting effect of antitoxin on sensitization by early doses of toxoid, the multiple doses of toxoid given at intervals during the period of decreasing passive immunity and the considerable delay in the development of active immunity all suggest that one of the later doses of toxoid may have initiated the sensitization and that the initial "simultaneous" toxoid may have been entirely without effect. Experiments were carried out to study this possibility.

EXPERIMENTAL OBSERVATIONS ON "SIMULTANEOUS SEROVACCINATION" AND DELAYED IMMUNIZATION AFTER ANTITOXIN

These were planned on the hypothesis that, since the presence of an excess of passive antitoxin inhibits the production of active immunity with toxoid, the stimulation of active antibodies will occur only when the passive immunity has reached a low level. If this is correct, there is an optimum time after passive immunization at which the inhibition disappears and the stimulation of an active immunity becomes effective, while toxoid given before this time is rendered inert by the heterologous antitoxin. Several properly spaced injections of toxoid, delayed until the approximate time of low passive immunity, would therefore be as effective as when the toxoid was started simultaneously with the antitoxin injection. For this it seems preferable to use alum toxoid, which is insoluble and presumably is dissolved and absorbed slowly and continuously over a period of time, so that antigen will become available for the stimulation of an active immunity as soon as the inhibition by antitoxin disappears. It is apparent that when smaller amounts of antitoxin have been given a shorter delay in starting toxoid is indicated than after large doses.

The effect of "simultaneous serovaccination" was compared with that resulting from a delay in the start of toxoid immunization for two, four and six weeks after the antitoxin injections in the following manner:

Twelve healthy children (from the Shriner's Hospital) were each given 10,000 units of tetanus antitoxin intramuscularly and separated into four groups of 3.

GROUP 1.—Each child was given 0.5 cc. of alum precipitated tetanus toxoid subcutaneously at the time of the antitoxin injection and every two weeks thereafter for a total of six injections.

GROUP 2.—Toxoid was started two weeks after the antitoxin and continued every two weeks for a total of five injections.

15. Sacquépée, E., and Jude, A.: Sur la valeur et la durée de l'immunité antitétanique après injection de rappel, chez l'homme immunisé contre la tétanos par l'emploi simultané du sérum et de l'anatoxine tétanique, Compt. rend. Soc. de biol. **125**: 711 (June 26) 1937.

GROUP 3.—Toxoid was started four weeks after the antitoxin and given again every two weeks for a total of four injections.

GROUP 4.—Toxoid injections were delayed until six weeks after the antitoxin, and a total of three doses was given.

An additional group of 3 children (group 5) was given only 1,500 units of antitoxin and toxoid was started two weeks later and continued at two week intervals for a total of five doses.

The observations covered a period of twelve weeks and antitoxin titrations were done on the blood of each child at the start of the experiment and at two week intervals thereafter.

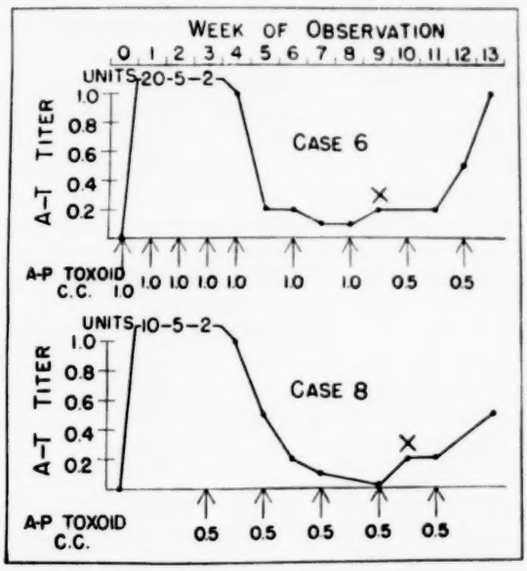
The observations in these five groups have been collected in table 4, in which the biweekly antitoxin titrations are shown. The early high levels of antitoxin fell gradually, and the variation observed in the rate of disappearance of antitoxin in different children could not be related to a previous dose of horse serum, since only 1 child (group 5, case 2) had had such an injection (diphtheria antitoxin). The complete destruction of 10,000 units of antitoxin within two weeks of its injection in 1 child (group 3, case 1) was quite unexplained, since she had received no previous horse serum. This child had severe serum sickness seven days after the antitoxin injection, but this occurred also in 7 other children in the series. The earliest increase in antitoxin titer is indicated in heavier type and is taken as the first development of an active immunity.

The results in this series also appear quite clearcut and definite. It will be noted that in the first four groups of children passively immunized with 10,000 units of antitoxin, all began to have an active immunity from the 8th to the 12th week of observation. While there was some inconstancy in the onset of active immunity in the different groups, this variation was no greater than that shown by the children in the same group. In these children, then, an active immunity developed at approximately the same time, whether the toxoid was started simultaneously with the antitoxin injection or two, four or six weeks later. On the other hand, one of the relatively constant and striking features was the low titer of passive antitoxin reached before the appearance of an active immunity. This was 0 in 7 children, 0.017 unit in 3, 0.01 unit in 1 and 0.05 unit in 1, which suggests that the disappearance of the inhibiting effect of passive antitoxin is more important in the early development of active immunity than the time at which the immunization is started. This is emphasized by the 3 children in group 5, each of whom was passively immunized with only 1,500 units of antitoxin. In them the passive immunity disappeared more quickly than in those given larger doses and fell to 0 in from four to six weeks. Although toxoid was not started until two weeks after the antitoxin, active immunity had begun to develop in all six weeks later.

Further observations of a comparison between "simultaneous serovaccination" and delayed immunization were possible on 2 children with clinical tetanus each of whom was given 100,000 units of antitoxin (cases 6 and 8). The detailed data of these 2 children are given in the protocols at the end of the paper, but a graphic representation of the results is shown in the accompanying chart. In case 6 active toxoid immunization was started simultaneously with the antitoxin injection and continued once weekly for five injections and thereafter once every two weeks. In case 8 toxoid was first given three weeks after the antitoxin and again every two weeks afterward. Antitoxin titrations were done at weekly intervals during a period of thirteen weeks and are expressed in units.

The antitoxin curves in these 2 cases show a striking similarity. From an early level of 20 to 40 units the titers fell to 1 unit at the end of four weeks and to 0.1 unit at seven weeks. In the first child (case 6) in whom toxoid immunization was started simultaneously with the antitoxin, the first demonstrable increase in antitoxin (active immunity) appeared nine weeks later following the seventh toxoid injection, while in the second child (case 8) in whom the toxoid immunization was delayed for three weeks an active immunity developed in the 10th week of observation following the fourth toxoid injection. In both instances the appearance of an active immunity was delayed until the passive immunity had reached a low level, and the early toxoid injections in the first case produced no appreciable acceleration in its development.

These results tend to confirm the relative inefficacy of toxoid given during moderate and high concentrations



Transition from passive to active tetanus immunity (indicated by X) after 100,000 units of antitoxin. Comparison of simultaneous serovaccination (case 6) with delayed toxoid immunization (case 8) by blood antitoxin titer.

of passive antitoxin and suggest that only when such passive immunity has reached a relatively low titer is active immunization with toxoid effective. They give no support to the value of "simultaneous" serovaccination and indicate that a transition from passive to active immunity is readily accomplished by delaying the start of active toxoid immunization from two to four weeks after the passive immunization, depending on the dose of antitoxin given.

SUMMARY

In a study of active and passive tetanus immunity on 39 children on whom more than four hundred tetanus antitoxin titrations were done, the following observations were made:

1. Although passive immunization with the usual prophylactic dose of 1,500 units or less produces an immunity of only approximately three weeks, larger doses cause a much more prolonged immunity. After the administration of 100,000 units or more it was found that the blood serum showed as much as 1 unit per

cubic centimeter for from three to four weeks, 0.1 unit from six to ten weeks and 0.01 unit from eight to eleven weeks. With a dose of 10,000 units the passive immunity was somewhat less prolonged, although in most instances 0.1 unit persisted for from four to six weeks and 0.01 unit from six to ten weeks.

2. Antitoxin in the spinal fluid of 2 children was determined during passive immunization. In 1 the spinal fluid contained 0.2 unit per cubic centimeter when the blood antitoxin titer was 30 to 50 units, while in the second the spinal fluid titer was 0.017 unit and the blood 70 units.

3. In 4 children with clinical tetanus it was observed that not only did antitoxic immunity not follow recovery but the amount of antigen (toxin) absorbed during a tetanus infection was so small as to produce no primary antigenic stimulus or "sensitization" to later active tetanus immunization.

4. Repeated subcutaneous or intracutaneous injections of tetanus toxoid did not produce an antitoxic immunity within several weeks. Such injections are of value in tetanus prophylaxis only when the subject has had one or more previous "sensitizing" toxoid inoculations.

5. When passive immunization was produced with 10,000 units or more of antitoxin, multiple injections of toxoid given subcutaneously or intracutaneously during the week following had no demonstrable immunologic effect. Such subjects did not have any active immunity for a period of many weeks and even when given a later "stimulating" dose of toxoid failed to respond by producing antitoxin. Control groups of children given toxoid in the same manner without being passively immunized reacted to the later dose by developing an active immunity in a short time. It was concluded that the presence of any considerable quantity of heterologous antitoxin prevents the usual "sensitization" of the body cells by toxoid and renders it inert as an antigen.

6. A passive immunity can be converted into an active immunity by toxoid injections. It was observed, however, that this transition can be produced as readily and as rapidly when the initial active toxoid injection is delayed several weeks as when it is started simultaneously with the antitoxin injection. After passive immunization with 10,000 units of antitoxin and with toxoid injections at two week intervals an active immunity developed in from eight to twelve weeks regardless of whether the first toxoid was given simultaneously with the antitoxin or whether it was delayed two, four or six weeks. The same similarity of active antitoxin response was found in 2 children passively immunized with 100,000 units. In 1 of them toxoid was started simultaneously with the antitoxin injection, while in the other the initial injection was delayed three weeks, but in the two the active immunity developed at about the same time.

It was concluded that these results were explained by the previously mentioned observations of the inhibition of larger amounts of heterologous antitoxin on the antigenic action of toxoid and that only when such passive antitoxin titers have reached a relatively low level is active toxoid immunization effective. This hypothesis was supported by the observation that a much more rapid active immunity could be produced after passive immunization with only 1,500 units of antitoxin. Under such circumstances the passive antitoxin titer falls more quickly, and children in whom toxoid was started two weeks after the antitoxin injection had an active immunity more quickly than those who had received larger doses (10,000 units) of antitoxin. These observations tend to refute the value of "simultaneous serovaccination" in the production of active tetanus immunity and show that a delay of active immunization of from two to four weeks following the antitoxin injection is indicated.

BRIEF PROTOCOLS OF CASES OF CLINICAL TETANUS IN WHICH IMMUNITY STUDIES WERE MADE

All 9 children in this group recovered except 1. They were given avertin with amylene hydrate for varying periods, but the details of therapy are omitted. All lived in rural or suburban localities at some distance from St. Louis, and in some of them prolonged observation was not possible. The immunologic data are collected in table 1 and those on cases 6 and 8 shown graphically in the chart.

CASE 1.—Ruby C., aged 5 years, with tetanus of four days' duration, was given 200,000 units of antitoxin intramuscularly over a period of four days. Twelve days after the last serum was given the blood showed 20 units and five days later 10 units. No further tests were done.

CASE 2.—Noreen B., a girl aged 8 years with tetanus of three days' duration, was given 90,000 units of antitoxin intravenously and 10,000 units subcutaneously on the first day of observation and 50,000 units intravenously two days later. Alum precipitated tetanus toxoid was given subcutaneously each day for the first seven days in 0.5 cc. doses. On the 3d day the blood showed 50 units of antitoxin and the spinal fluid 0.2 unit; on the 9th day the titer was 30 units in the blood and still 0.2 unit in the spinal fluid. Examination of the blood showed 20 units on the 13th day, 10 on the 18th, 0.5 on the 30th day and 0.1 on the 68th. On the 74th day, 1 cc. of alum precipitated toxoid was given subcutaneously and six days later (80th day) the antitoxin titer was 0.017 unit while on the 125th day it had fallen to 0.003. At this time another dose of 0.5 cc. of alum precipitated toxoid was given subcutaneously. Two months later (177th day) 0.5 unit was found in the blood, and a final dose of 0.5 cc. of alum precipitated toxoid was injected subcutaneously with the development of an antitoxin titer of 5 units two weeks afterward (185th day).

CASE 3.—Ruth R., aged 10 years, with clinical tetanus of eight hours' duration, was given 20,000 units of antitoxin intravenously and 30,000 units intramuscularly on the first day of observation and 50,000 units intramuscularly the day following. Daily doses (0.5 cc.) of toxoid, alum precipitated, were given intracutaneously for the first seven days. The serum titers of antitoxin showed the following: 3d and 4th days 20 units, 5th to 10th day 10 units, 12th day 7.5 units, 15th day 5 units, 20th and 24th day 2.5 units, 27th and 32d day 1.0 unit, 37th day 0.5 unit, 47th day 0.2 unit, 57th day 0.1 unit, 76th day 0.017 unit and 111th day less than 0.003 unit. On this day 1 cc. of alum precipitated tetanus toxoid was given subcutaneously, and seven days later (118th day) the blood still showed no antitoxin, although thirty days after this injection (141st day) the serum titer was 0.2 unit. No further observations were made for five and one-half months, at which time the blood showed 0.05 unit. A final dose of 1 cc. of plain toxoid was given subcutaneously and the antitoxin increased to 2 units after one week and to 5 units after two weeks.

CASE 4.—Clement H., a boy aged 13 years, with clinical tetanus, was given 100,000 units of antitoxin on the first day of observation. The serum antitoxin titers were as follows: 4th day 20 units, 9th day 10 units, 14th day 5 units, 29th day 0.5 unit, 43d day 0.1 unit, 57th day 0.01 unit, 85th day less than 0.003 unit. One month later, the blood still

showed no antitoxin, and 1 cc. of plain tetanus toxoid was given subcutaneously. After two months the titer was still less than 0.003 unit.

CASE 5.—Charles K., a boy aged 13 years, with clinical tetanus, received 50,000 units of antitoxin intravenously the first day of observation and 50,000 units by the same route the day following. On the 3d day the serum showed 30 units, on the 17th day 2 units and on the 24th day 1 unit. No further observations were possible.

CASE 6.—Geneva G., a Negro girl aged 3 years, was burned severely over the abdomen and legs. Clinical tetanus developed eighteen days later for which she was given 40,000 units of tetanus antitoxin intravenously and 60,000 units intramuscularly together with 1 cc. of alum precipitated tetanus toxoid subcutaneously. She received weekly subcutaneous injections of alum precipitated toxoid during the next four weeks (five injections), and these were continued at biweekly intervals subsequently. Antitoxin titrations of the blood done weekly are shown in table 5.

TABLE 5.—*Weekly Antitoxin Titrations of the Blood*

Day of Observation	Blood Antitoxin Titer, Units	Alum Precipitated Toxoid, Cc.
0-1	0	1
7	20	1
14	5	1
21	2	1
28	1	1
35	0.2	..
42	0.2	1
49	0.1	..
56	0.1	1
63	0.2	..
70	0.2	0.5
77	0.2	..
84	0.5	0.5
91	1.0	..

TABLE 6.—*Antitoxin Titrations (Case 8)*

Day of Observation	Blood Antitoxin Titer, Units	Alum Precipitated Toxoid, Cc.
0-1	0	...
4	40	...
9	10	...
14	5	...
21	2	0.5
28	1	...
35	0.5	0.5
42	0.2	...
49	0.1	0.5
63	0.017	0.5
70	0.2	...
77	0.2	0.5
91	0.5	...

CASE 7.—Raymond N., a boy aged 7 years, with very severe tetanus, was given 50,000 units of antitoxin intravenously and the same amount intramuscularly. The following day his blood showed 70 units per cubic centimeter and the spinal fluid 0.017 unit. Death occurred on the second day, apparently from peripheral circulatory collapse.

CASE 8.—Mary W., aged 6 years, with clinical tetanus, received 100,000 units of antitoxin, half intramuscularly and half intravenously. Active immunization with toxoid was started three weeks later. The antitoxin titrations are shown in table 6.

CASE 9.—Clyde C., a boy aged 6½ years, had mild clinical tetanus of two weeks' duration when first seen and was given no antitoxin. His blood showed no antitoxin when examined on the 4th, 13th, 20th and 37th days of observation. On the 37th day he was given 1 cc. of tetanus toxoid subcutaneously and no antitoxin developed by the 44th, 51st or 100th day.

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THE SYNDROME OF UNILATERAL RUPTURE OF THE SIXTH CERVICAL INTERVERTEBRAL DISK

WITH COMPRESSION OF THE SEVENTH CERVICAL NERVE ROOT

A REPORT OF FOUR CASES WITH SYMPTOMS SIMULATING CORONARY DISEASE

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Rupture of a cervical intervertebral disk into the spinal canal has been reported many times. With few exceptions, however, the symptoms were due to compression of the spinal cord rather than the nerve roots. Adson,[1] Elsberg,[2] Stookey,[3] Peet and Echols,[4] Mixter and Ayer,[5] Hawk,[6] Love and his co-workers[7] and Bradford and Spurling[8] all have reported 1 or more cases of rupture of the cervical disks. Of all these cases only 4 seem to have had nerve root compression without involvement of the spinal cord, and of these 1[9] was a rupture of the sixth disk. In this particular case the description of the exact radiation of the pain and of the sensory findings was quite limited. Two of the cases[10] were not proved pathologically, but there seems to be very little doubt of the diagnosis.

From a review of the literature, therefore, it would seem that most of the ruptured disks in the cervical spine produce either bilateral or unilateral cord pressure and that disks causing nerve root symptoms alone are very rare. Indeed, such statements have been made by several of the authors who have written on this subject, namely Stookey,[11] Love and Walsh[12] and Bradford

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Since this paper was written, 7 additional cases have been seen. Four of these have been proved at operation. The remaining 3 have not yet come to operation.

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9. Stookey, Byron: Compression of the Spinal Cord Due to Ventral Extradural Cervical Chondromas: Diagnosis and Surgical Treatment, Arch. Neurol. & Psychiat. **20:** 275-291 (Aug.) 1928.

10. Mixter and Ayer.[5] Bradford and Spurling.[8]

11. Stookey, Byron: Compression of Spinal Cord and Nerve Roots by Herniation of the Nucleus Pulposus in the Cervical Region, Arch. Surg. **40:** 417-432 (March) 1940.

12. Love, J. G., and Walsh, M. N.: Protruded Intervertebral Disks: A Report of One Hundred Cases in Which Operation Was Performed, J. A. M. A. **111:** 396-400 (July 30) 1938.

and Spurling.[8] We believe, however, that exactly the reverse is true. We believe further that an undetermined number of patients with pain in the precordium, in the shoulder and in the arm, who heretofore were thought to have coronary thrombosis, angina pectoris, arthritis of the cervical spine, brachial plexus neuritis and neuralgia, bursitis, scalenus anticus syndrome, cervical rib or discogenetic disease will be found to have a rupture of one of the lower cervical disks.

Unilateral rupture of the sixth cervical disk with compression of the seventh cervical nerve root causes as definite a syndrome as similar lesions of the fourth and fifth lumbar disks. This report is based on 3 such cases proved at operation. One other case as yet unverified by operation is included, because the similarity of the history and physical findings to the 3 proved cases makes the diagnosis almost certain. All 4 cases are practically identical.

ANALYSIS OF CASES

Three of the patients were men and 1 was a woman. Two of the patients were physicians. The youngest was 40 years of age and the oldest 51. In all cases the pain was on the left side. The duration of symptoms varied from seven years to three weeks.

Each patient gave a history of numerous cricks in the neck recurring intermittently for months or years preceding the attack of radiating pain. The onset was precipitated in 1 case when the neck was jerked suddenly while the patient was driving a car and in another when the patient bent over to tie his shoe. In the 2 remaining cases there was no definite movement or injury to which the onset could be attributed. Each patient had a particularly severe crick in the neck before the rather sudden onset of the disabling pain. The pain radiated in each case to three general regions: (1) the precordium, (2) a point just medial to the upper angle of the scapula and (3) down the lateral and medial surfaces of the arm. In each instance there was considerable difficulty in breathing and a sense of impending death and in 1 case cyanosis. At the beginning of the attack, the pain in the precordium was most intense and every patient thought that he had had a heart attack. After a few days or weeks this pain abated to some extent and that in the rhomboid region and arm became more pronounced. All pain was intensified by moving the neck, sneezing, coughing and straining. Three patients complained of definite numbness and weakness in the index finger and slight numbness in the middle finger. The same 3 patients also stated that the involved arm was always cold.

Examination showed severe muscle spasm in the neck and shoulder. The neck was held rigidly and abduction of the neck from the side of the lesion caused an exacerbation of the pain, while traction on the head relieved the symptoms to some extent. In each patient there was an exquisitely tender point just posterior to the scalenus anticus muscle over the exit of the seventh cervical nerve from the spinal canal. There was also a point of tenderness over the painful area in the rhomboid region. In 3 cases pronounced hypesthesia and hypalgesia were found over the entire index finger, which extended to the metacarpophalangeal joint. In these same 3 cases there was slight reduction of sensation in the middle finger. In 1 case no objective sensory disturbance was found. In 3 cases there was weakness in the movement of the index finger, particularly in flexion. The reflexes were normal in all cases and there was no evidence of muscular atrophy. There were no findings in any case suggestive of spinal cord pressure, although 1 patient had a conditional tremor in the opposite hand, which is still unexplained.

X-ray examination of the cervical spine showed a straightening of the cervical curve in each instance. There was no evidence of hypertrophic arthritis in any of these cases at the beginning of symptoms. In 1 case, however, reexamination of the neck seven years after the onset and shortly before operation showed narrowing of the fifth and sixth disks with lipping of the edges of the adjacent vertebrae. Another patient is beginning to show spur formation on the sixth and seventh vertebrae one year after the operation.

Lumbar puncture was performed on all 4 patients. The total protein was increased in 2 and was normal in 2. The dynamics of the fluid were normal in all 4 cases.

The diagnosis of this condition was made solely on the basis of the history and physical findings. No contrast medium in the spinal canal was used by us, although in 1 case iodized poppy seed oil had been injected elsewhere with negative results. In this case and in 1 other, the ruptured disk was so far out in the intervertebral foramen that the nerve alone was compressed. Contrast mediums could not have shown these lesions, but in a third case there was some slight indentation of the dura which might have produced a filling defect.

The operative procedure was carried out under local anesthesia. The lower cervical laminas on the side of the lesion were exposed and the involved nerve root was identified by the patient when gentle pressure was applied on the ligamentum flavum, reproducing the exact pain. In each instance the ruptured disk was found directly beneath. This test was made before any bone was removed, eliminating the necessity of exploring several interspaces. A small portion of the adjacent laminas was removed and the interlaminar portion of the ligamentum flavum was excised. As this was done, the nerve root came into view, pushed up against the ligamentum flavum and was flattened out by the nodule of disk.[13] The nerve root then was injected with procaine hydrochloride and, almost instantaneously, all pain was relieved. Approximately half of the articular facets and the capsular portion of the ligamentum flavum were removed, and the nerve root was retracted upward or downward, exposing the nodule of disk without difficulty. These herniated disks differed from those found in the lumbar region only in size, being smaller than the latter. The loose fragments of fibrocartilage were removed, thus relieving the pressure on the nerve.

Two of the 3 patients operated on now are relieved completely of all of their original pain; whereas the third, although relieved of the shoulder pain, still has some discomfort in the arm and occasional pain in the precordium. He states, however, that this is not nearly as intense as before the operation and feels that the operation was well worth while. The patient who was not operated on was seen by us before the cause of her pain was recognized. She gradually has improved to the point at which she is able to continue her work but still has occasional pain at intervals, especially after periods of activity.

13. It should be remembered that in the cervical region the nerve roots emerge from the dura at the level of the foramens through which they make their exits and are compressed as they go through the foramens, whereas in the lumbar region the nerve roots come out of the dura and are compressed by the ruptured disks a segment above the points of their exit from the canal.

REPORT OF CASES

CASE 1.—*History of cricks in neck for three years prior to onset of severe pain in neck, rhomboid region, arm and precordium, which lasted seven years; injection of iodized oil with negative results; scalenus anticus section without relief; removal of rupture of sixth cervical disk with partial relief of symptoms.*

History.—J. W. B., a white man aged 41, a surgeon, admitted to the Willis Campbell Clinic on Aug. 2, 1933, complained chiefly of violent pain in the left side of the neck, the precordium, the rhomboid region and the left arm. During the last three years the patient had had three very severe cricks in the left side of the neck.

Three weeks before admission the patient had a severe crick in the neck and a few days later experienced intense pain associated with muscle spasm in the left rhomboid region. A short time thereafter an extremely violent radiating pain occurred in the precordium and down the left arm. This pain completely incapacitated him and he spent most of the time in bed, taking large doses of codeine and soluble pentobarbital. One week before admission he consulted an internist because he thought he had a coronary occlusion with an atypical distribution of pain. Complete investigation of the heart, however, failed to reveal any evidence of coronary disease.

Examination.—The neck was held rigidly and there was considerable muscle spasm in the left rhomboid region. There was definite tenderness over the brachial plexus and over the painful area in the rhomboid region. There was no weakness in the hand nor was there any change in sensation in the arm or fingers. All reflexes were normal.

X-ray examination of the cervical spine showed that it was held in slight flexion but was otherwise negative.

Diagnosis.—Brachial plexus neuralgia, cervical arthritis and like conditions were considered.

Course.—Injection of procaine hydrochloride into the brachial plexus, head traction and a Thomas collar were tried, with only temporary relief. The pain continued in such intensity that it was impossible for him to continue his practice. Many internists, neurologists and neurosurgeons in various parts of the country were consulted in the next six or eight months. At one clinic an exploration of the rhomboid region was made, which was entirely negative. During the next three years he spent his winters in Arizona and summers in Wisconsin, where he thought the pain was less severe than at his home in Arkansas. A conditional tremor of the right arm and hand developed during this period. During the winter of 1937 the pain again became almost unbearable and he was referred to yet another neurosurgical clinic for investigation.

Neurologic examination was again entirely negative, but examination of the spinal fluid showed a consistently high total protein of 60 mg. per hundred cubic centimeters, and it was felt that there was some pressure on the fifth or sixth cervical nerve root. Intraspinal injection of iodized poppy seed oil was carried out with negative results. The tremor in the right arm was thought to be functional. In 1938 the patient returned to Memphis and a section of his scalenus anticus muscle on the left was carried out without relief of symptoms.

In September 1940 the patient experienced an exacerbation of the pain so intense that he was certain this time that he did have a coronary occlusion. Again investigation of his heart failed to reveal any abnormality. There was no change in the neurologic findings, and the spinal fluid protein was again found to be 60 mg.

X-ray examination at this time showed a very definite narrowing of the fifth and sixth cervical disks with considerable spur formation along the edges of the fifth, sixth and seventh cervical vertebrae.

It so happened that the patient's return to Memphis for investigation coincided with the admission of L. G. (case 2) to the John Gaston Hospital. Comparison of the symptoms and physical manifestations in these 2 cases showed that they were identical, with the exception of the lack of sensory change in the first case. Five days after the removal of the sixth cervical disk in case 2, J. W. B.'s sixth cervical disk was explored and a very definite rupture of the disk was found and removed. When the seventh cervical nerve root was injected with procaine hydrochloride, the relief of pain was instantaneous; the index finger became almost anesthetic and the middle finger hypesthetic. Some pain in the arm recurred immediately following the operation. The pain in the neck and in the rhomboid region was relieved entirely and only occasionally did he have any pain in the precordium.

One year after the operation the patient writes that he has felt fairly well during the summer. He still has moderate pain in the arm and occasional pain in the precordium, which is brought on by exertion. He feels that, although he is not relieved entirely, the operation has been well worth while. The conditional tremor in the right arm continues and is still unexplained.

CASE 2.—*History of cricks in neck intermittently for three or four years, followed by violent pain in the left shoulder, precordium and left arm for two weeks; removal of rupture of sixth cervical disk with complete relief.*

History.—L. G., a white man aged 45, a carpenter, admitted to the John Gaston Hospital Sept. 17, 1940, complained chiefly of a crushing pain in the neck, precordium, shoulder and arm.

For the last three or four years the patient had had frequent cricks in the neck which lasted only a few days and had not been incapacitating. In addition, he had had occasional sharp pains in the precordium and left arm, which lasted only a few minutes at a time.

Two weeks before admission the patient bent over to tie his shoe and was seized suddenly with a violent pain in the left side of the neck, which radiated into the heart, the left shoulder and the left arm. The pain was so intense that at times it was difficult for him to breathe. He called a physician, who gave him a large dose of morphine, with some relief. The following day, however, the pain was as intense as ever and he noticed that the index finger on the left hand was quite numb and that the middle finger was slightly numb. Since the onset the pain had been agonizing and completely disabling. He had been able to sleep very little except when under the influence of opiates. He noticed that any movement of the neck accentuated the pain and that supporting the left arm with the right gave him some relief. Coughing, sneezing or straining aggravated the symptoms. Since the onset of pain the patient had noticed that his left hand and arm felt cold all the time.

Examination.—The patient was in obvious pain. The neck was held rigidly toward the left and slightly forward. The left arm was supported by the right. Passive movement of the neck or traction on the involved arm intensified the pain. There was considerable muscle spasm in the neck and in the left shoulder, and there was a point of definite tenderness over the brachial plexus just posterior to the scalenus anticus muscle. The entire left index finger was almost completely anesthetic, and there was moderate hypesthesia of the left middle finger. There was slight weakness of the index finger on flexion but no other weakness in the arm. The reflexes were normal and no temperature change in the arm was noticed. Blood pressure was the same (125 systolic and 85 diastolic) in both arms and the radial pulse was felt easily.

X-ray examination of the cervical spine showed a loss of the normal cervical curve but was otherwise negative.

Spinal fluid examination showed normal dynamics and a total protein of 50 mg. per hundred cubic centimeters.

The diagnosis was rupture of the fifth or sixth cervical intervertebral disk.

Course.—An exploration of the spinal canal was advised. To this the patient readily agreed, stating that he could not bear the pain much longer.

On September 24 a subtotal hemilaminectomy was performed. When the ligamentum flavum between the sixth and seventh cervical laminas on the left was pressed on, the old pain was reproduced in all its intensity. A small part of the adjacent laminas was removed and when the ligamentum flavum was dissected out the seventh cervical nerve root was exposed. It was pushed backward and flattened out by rupture of the sixth disk. The loose fragments of fibrocartilage were removed without difficulty, and the nerve root was completely decompressed.

Following the operation the patient was entirely relieved of all of his pain and has remained so to the present time. The muscle spasm in the neck and shoulder subsided as the sore-

ness from the operative wound diminished and the sensory disturbance in the index and middle fingers began to clear up.

One year after the operation the patient states that he never has any more pain in the left arm, shoulder or precordium but recently has begun to have a little pain in the right side. The left index finger is still slightly hypesthetic over the distal phalanges; the middle finger is entirely normal. X-ray examination of the cervical spine now shows beginning spur formation along the edges of the sixth and seventh cervical vertebrae.

CASE 3.—*Three year history of cricks in the neck, culminating in a violent attack of pain simulating coronary occlusion; removal of rupture of sixth cervical disk with complete relief of pain.*

History.—R. B. McC., a white man aged 47, a pediatrician, admitted to the Baptist Memorial Hospital Aug. 16, 1941, complained chiefly of violent pain in the neck, precordium, left shoulder and left arm.

For the past seven years the patient had had attacks of mild precordial pain with no radiation whatever. Electrocardiograms had been made during this period which failed to reveal any changes suggestive of coronary disease. For the past three years the patient had had twenty or thirty cricks in the left side of the neck. Neither of these disturbances, however, incapacitated him, and he was able to carry on a very active practice.

Three weeks before admission, while driving his car, the patient received a severe jar to his neck. A few hours later what he thought was a typical crick in the left side of the neck developed. Three days later, while playing pool, he missed the cue ball entirely, again jerking his neck forward, and instantly experienced such an agonizing pain in the neck that it almost knocked him down. The pain radiated to a point just medial to the upper angle of the left scapula and continued throughout his illness.

On the day before admission he noticed a burning sensation in his left arm from the elbow to the finger tips. A few hours later his left index finger became almost entirely anesthetic and the left middle finger became slightly numb. During the night before admission he was awakened by a violent pain in the left shoulder, precordium and left arm. After he had taken a sedative, the pain abated to a certain extent. Shortly after he arrived at his office the next morning, the pain again became so violent that he was able to breathe only with the greatest difficulty. Several physicians were summoned hurriedly and they found the patient in excruciating pain, quite cyanotic and breathing with considerable difficulty. The blood pressure was 132 systolic and 80 diastolic. The heart was regular with a rate of 70.

He was given a quarter of a grain (0.016 Gm.) of morphine sulfate and as soon as the pain subsided to some extent he was moved to the Baptist Memorial Hospital. When he lay down in bed the pain almost disappeared, but when he sat up it would recur. An electrocardiogram was made on admission and revealed the following abnormalities: In lead 1 the T wave was barely above the isoelectric line. In lead 4 the R wave was 3 mm. in height; otherwise, the tracings were normal. It was felt that he had coronary occlusion, and during the next three days he was kept in an oxygen tent most of the time. The pulse ranged from 66 to 90. There was no fever, no shock, no pericardial friction rub, no leukocytosis or any other constitutional evidence of infarction. On the second hospital day another electrocardiogram showed that the T waves in leads 1, 2 and 3 had become flattened and that the R wave in lead 4 was 3 mm. in height, as before. On the third day after admission it became increasingly evident that the pain was not that of coronary occlusion but was explainable on the basis of involvement of the cervical nerves. Five days after admission we were called in to see the patient.

Examination.—The neck was held rigidly and slightly to the right. There was definite muscle spasm in the left side of the neck and in the left shoulder. Any movement of the neck precipitated a severe attack of pain and traction downward on the left shoulder did likewise. Traction on the head gave considerable relief. There was a point of exquisite tenderness over the brachial plexus just posterior to the scalenus anticus muscle and one of moderate tenderness over the scalenus anticus muscle itself on the left. There was also a tender area just medial to the upper angle of the scapula over the left rhomboidei muscles. There was some weakness of the left index finger, particularly on flexion. Sensory examination showed almost complete anesthesia of the entire left index finger and slight reduction of sensation in the left middle finger. The reflexes were normal and the blood pressure in the two arms was the same.

X-ray examination showed loss of the cervical curve but otherwise was negative.

Spinal fluid examination showed normal dynamics, normal cell count and a total protein of 25 mg. per hundred cubic centimeters.

The diagnosis was rupture of the sixth cervical disk with compression of the seventh cervical nerve root.

Course.—Head traction was applied. This was followed by considerable relief of pain for several days. Injection of procaine hydrochloride into the painful area just medial to the upper angle of the scapula gave immediate and complete relief of all pain for several hours. Electrocardiograms on the seventh, ninth and seventeenth days after admission revealed a gradual return of normal pattern. Head traction was continued for about three weeks; however, during the latter part of this time the pain again became more intense and it was decided that removal of the disk should be undertaken.

On September 12, under local anesthesia, the laminas of the sixth and seventh cervical vertebrae on the left were exposed. Pressure on the ligamentum flavum between the sixth and seventh cervical laminas immediately reproduced all of the old pain. Approximately half of the sixth and seventh cervical laminas was removed and the ligamentum flavum dissected out, revealing the seventh cervical nerve root pushed backward against the edge of the articular facets and the remaining ligamentum flavum by a small mass approximately a quarter of an inch in diameter. The nerve root was injected with procaine hydrochloride and about half of the articular facets removed. The nerve root then was retracted upward, revealing a typical ruptured disk. The capsule of the disk was incised and three small fragments of loose fibrocartilage were lifted out. Following this, the nerve root was quite free in all directions and no attempt was made to remove the remainder of the nucleus between the vertebrae.

Since the operation, the patient has been entirely free of pain. The sensory disturbance of the index finger is improving while that of the middle finger has disappeared. Six weeks after the operation, he resumed his practice and has continued it without difficulty.

CASE 4.—*Agonizing pain in neck, left shoulder, precordium and left arm for three months; procaine injection of thoracic sympathetic ganglions and brachial plexus, diathermy and other therapy without relief; gradual recovery over a period of three years.*

History.—Mrs. F. S., a white woman aged 51, an organist, admitted to the Gartly-Ramsay Hospital May 26, 1938, complained chiefly of agonizing pain in the left side of the neck, left shoulder, left arm and precordium for three weeks. She had had occasional cricks in the neck for years.

Three weeks before admission to the hospital, the patient had a severe pain in the left side of her neck which radiated to the base of the skull. Two days later, while driving her car, she experienced a sudden violent pain which shot from the neck into the precordium to the shoulder and down the medial and lateral aspects of the left arm to the finger tips. Pain was so intense that she could hardly breathe, and she was quite certain that she had a heart attack and surely would die. She was taken home and put to bed, where much to her surprise the pain was relieved to a considerable extent but would recur as soon as she assumed the upright position. Her physician who was called felt that she did not have a heart attack but rather some type of neuritis of the brachial plexus. Large doses of opiates were given, with partial relief. The following morning the patient noticed that there was no feeling in the entire left index finger and that she could move it only with the greatest difficulty. There was also some numbness in the left middle finger. The pain soon became constant, whether the patient was in the upright or the prone position.

Complete investigation of the heart, including an electrocardiogram, was negative. She was given numerous diathermy treatments to the neck, shoulder and arm with little relief.

Examination.—Three weeks after the onset of symptoms, the patient was in severe pain. The neck was held toward the left and the left arm was supported by the right. Any movement of the neck to the right or traction on the left arm accentuated the pain. There was considerable muscle spasm in the neck and in the left shoulder girdle. There was exquisite tenderness over the brachial plexus posterior to the scalenus anticus muscle as well as over the scalenus anticus itself. The left index finger was almost completely anesthetic, anteriorly and posteriorly, and sensation was reduced in the middle finger. The index finger could be moved only with the greatest difficulty. Complete flexion of this finger could not be carried out. There was no other weakness of the arm or hand and no disturbance of the reflexes could be made out.

X-ray examination of the cervical spine was negative except for loss of the cervical lordosis.

Spinal fluid examination showed normal dynamics, cell count and protein and the Wassermann reaction was negative.

Diagnosis.—A rupture of one of the lower cervical intervertebral disks was suspected at the time, but it was felt that the pain in the heart could not be explained on this basis.

Course.—Procaine injection of the scalenus anticus muscle, the cervical plexus and the first five thoracic sympathetic ganglions failed to relieve the pain. Diathermy, massage and large quantities of opiates were continued for several weeks, after which time the pain began to abate. Since then there has been gradual improvement in her symptoms, until in the last six months she has been relatively free of pain; however, when she becomes tired after considerable activity the old pain recurs for a short time.

Examination on Sept. 29, 1941 failed to reveal any muscle spasm in the neck or shoulder. Pressure over the seventh cervical nerve root, however, still reproduced the pain. There was no weakness in the arm, all reflexes were normal and the sensation in the index and middle fingers had returned to normal. The patient now continues her occupation as a church organist without difficulty.

COMMENT

Descriptions of this syndrome have appeared in the literature from time to time during the last few years, but no one to our knowledge has proved before that it could be due to a rupture of one of the lower cervical intervertebral disks. Nachlas [14] in 1934 described a syndrome of pseudoangina pectoris originating from demonstrable hypertrophic changes in the cervical spine. He felt that the irritation and compression of the cervical nerve root, secondary to these arthritic changes, were the cause of the radiating pain. Hanflig [15] in 1936 described a group of 30 cases presenting pain in the shoulder girdle, arm and precordium due to hypertrophic arthritis of the lower cervical spine. He thought that these cases were frequent and representative of a large group of persons with symptoms commonly classed as neuritis. Reid [16] in 1938 stated that pressure on the brachial plexus by a cervical rib and scalenus anticus muscle could cause pain simulating angina pectoris or coronary thrombosis. Numerous authors have reported cases somewhat similar to ours due to the scalenus anticus syndrome.[17]

Finally, in a series of papers which were published between 1936 and 1940, Turner and Oppenheimer [18] reported a series of 50 cases presenting symptoms quite like those reported by us. They believed that the arthritis which was found in the cervical spines of their patients was the result of thinning of the intervertebral disks and actually played no part in the production of symptoms. They cited the works of Keyes and Compere,[19] who showed that destruction of or injury to the intervertebral disk could produce hypertrophic arthritis. Turner and Oppenheimer believed that narrowing of the intervertebral foramens, which resulted from thinning of the intervertebral disk, caused the nerve root pressure. They called this condition discogenetic disease.

As a result of our experience with a large group of ruptured intervertebral disks in the lower lumbar region, we, like Turner and Oppenheimer, have come to believe that hypertrophic arthritis rarely causes nerve root pain. We are also in complete agreement with Keyes and Compere, having watched spur formation develop along the edges of vertebrae adjacent to a ruptured disk in several cases. We do not agree, however, that narrowing of the intervertebral foramens, which results from thinning of the intervertebral disks, often produces nerve root pressure. Such narrowing can occur only in the vertical diameter. Study of the foramens of the cervical spine is sufficient to convince one that this diameter is adequate for the passage of the nerve at all points even though the disk space is obliterated completely. Destruction of the adjacent surfaces of the vertebrae, however, which sometimes follows thinning of the disk, can result in further narrowing of the vertical diameter of the intervertebral foramens sufficient to produce constriction of the nerve. On the other hand, the horizontal diameter may become inadequate for the nerve root if there is any encroachment on it by the disk. This diameter is smallest at the points of maximum lordosis of the spine, namely the lower cervical and lower lumbar regions, and is the result of the projection of the articular facets toward the floor of the canal. The poker spine, which is seen in both the lumbar and the cervical ruptured disks, is probably an attempt of the body to increase the distance from the facets to the disk and thus relieve the pressure on the nerve root.

We do not wish to infer that all cases which heretofore have been diagnosed as cervical rib or scalenus anticus syndrome are ruptures of the cervical disks. It is undoubtedly true, however, that an undetermined number of these patients have ruptured disks. Two of our cases were diagnosed elsewhere as scalenus anticus syndrome. On the other hand, rupture of a cervical disk will cause spasm of the scalenus anticus muscle. (Note the spasm of the sacrospinalis and iliotibial band in ruptures of the lumbar disks.) The relief of symptoms following section of the scalenus anticus muscle in such cases might be explained on the same basis as the relief of pain from the Ober fasciotomy in the case of ruptured disk in the lumbar region.

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18. Turner, E. L., and Oppenheimer, Albert: A Common Lesion of the Cervical Spine Responsible for Segmental Neuritis, Ann. Int. Med. **10:** 427-440 (Oct.) 1936. Oppenheimer, Albert, and Turner, E. L.: Discogenetic Disease of the Cervical Spine with Segmental Neuritis, Am. J. Roentgenol. **37:** 484-493 (April) 1937. Oppenheimer, Albert: Discogenetic Disease, Am. J. Surg. **47:** 642-650 (March) 1940.
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Perhaps the most fascinating implication of this study is the possibility that many cricks in the neck are not, after all, the result of sleeping in a draft, some focus of infection or fibrositis, but are due to stretching or tearing of the annulus fibrosus of one of the cervical disks. Certainly in our 4 cases the numerous cricks in the neck of which these patients complained were in no way different from those seen almost daily. Perhaps it is not stretching the imagination too much to think that such a crick may be comparable to lumbago, which is doubtless the forerunner of ruptured disks in the lumbar spine in many cases.

Of all of the mistaken diagnoses made in this condition, that of coronary disease is most logical. It is not surprising that when a patient with agonizing pain in the heart and arm, associated with extreme difficulty in breathing, presents himself, the first thought is of coronary disease. The fact that the 2 patients who are physicians believed in the beginning of the attack that they had coronary occlusion is most significant.

Of particular interest is the sensory disturbance resulting from pressure on the seventh cervical nerve root. The degree of sensory loss of the index finger in these cases is out of all proportion to that which we have seen elsewhere in the trunk or extremities when a single spinal sensory root has been sectioned. This suggests that the seventh cervical nerve root is almost entirely responsible for the enervation of this finger, in many persons at least. Such a conception is at variance with the work of Head,[20] Foerster [21] and Sherrington [22] and is subject to further proof. The pattern of the sensory disturbance of the seventh cervical root is also different from that described by Sherrington [22] and Tilney and Riley,[23] being limited to the index and middle fingers without involvement of the thumb, the hand or the forearm.

The pathway of the radiation of pain to the precordial region is not definitely known. Nachlas [14] suggests that the mechanism of the reference of this pain is as follows: The pathway is along the lateral anterior thoracic and medial anterior thoracic nerves, the former originating in the sixth and seventh cervical segments and the latter in the eighth cervical and first thoracic segments. Although these nerves are known to be motor nerves, it has been well established that such nerves possess protopathic sensation so that pressure on them will produce definite pain, diffuse in character but referable to the terminal portions of the nerve. This and other possible pathways of the radiation of this pain are being investigated at the present time.

Herniation of one of the lower cervical disks was suspected for several years before it was confirmed finally in our first patient (case 1) because the symptoms and physical manifestations were analogous in every respect to those caused by ruptures of the lower lumbar disks. We now believe that the diagnosis can best be made by clinical means alone and that the use of contrast mediums is unnecessary, as we have previously shown in the diagnosis of ruptured disks in the lumbar region.[24] There is reason to believe that the percentage of error with contrast mediums will be even greater in the cervical spine than in the lumbar region. There are 3 causes for this: (1) The lesions are smaller, (2) they may be so far lateral that they are not in contact with the dura and (3) there is difficulty in filling the cervical canal with contrast mediums.

The presence of a unilateral rupture of one of the lower cervical disks is not in itself an indication for its removal unless it is causing incapacitating pain. Undoubtedly as this condition becomes more widely recognized many patients with pain less intense than that described here will be seen and will respond to more conservative measures. We recently have seen such a case which is not included in this report.

Unquestionably, the operative approach of choice is subtotal hemilaminectomy. It provides ample exposure and at the same time affords considerable protection to the spinal cord. It reduces also the postoperative soreness and possible weakness of the neck which might follow a complete laminectomy. We prefer local anesthesia in spite of the fact that there is some pain incident to exposure of the nerve root before it is injected with procaine hydrochloride. This anesthesia allows one to confirm the localization of the lesion before any bone is removed and affords further protection to the spinal cord. When the nodule of disk is exposed, only the loose fragments of fibrocartilage and those protruding from the disk space are removed. No attempt is made to curet out the remainder of the nucleus pulposus, as we do routinely in the lumbar region. Only the future will disclose whether this procedure is adequate for a permanent cure.

CONCLUSIONS

1. Unilateral rupture of the sixth cervical intervertebral disk produces a syndrome characterized by pain in the neck which radiates to the shoulder, precordium and arm and by sensory changes in the index and middle fingers.

2. The diagnosis of this condition can be made more accurately by clinical means than by the use of contrast mediums.

3. The operation of choice is subtotal hemilaminectomy under local anesthesia.

4. The localization of the lesion can be verified at operation before the removal of any bone.

5. Hypertrophic arthritis and/or narrowing of the intervertebral disk seldom causes nerve root pressure.

6. Rupture of any intervertebral disk may result in hypertrophic changes on the edges of the adjacent vertebrae.

7. The degree of sensory change in the index finger, which results from compression of the seventh cervical nerve root, in our experience, is more pronounced than that produced by interruption of any other single spinal nerve root.

8. The pathway over which the pain radiates to the precordium has not been ascertained.

9. An undetermined number of patients who heretofore have been thought to have coronary occlusion, angina pectoris, hypertrophic arthritis of the cervical spine, neuritis of the brachial plexus, bursitis, scalenus anticus syndrome or cervical rib have a rupture of one of the lower cervical intervertebral disks.

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THE USE OF PENTOTHAL SODIUM ANESTHESIA IN THORACIC SURGERY

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The selection of an anesthetic for thoracoplasties presents a problem differing from that in other types of surgery in that the patient is more or less debilitated by long-standing infection and there is apt to be damage to the kidneys, liver and heart owing to the effects of prolonged toxemia or involvement with tuberculosis. The most important difference is the presence of infection in the lungs and the necessity of avoiding irritating inhalants which might in any way adversely affect the pulmonary lesions. The administration of ether by the drop method is not recommended because of its irritating effect on the mucous membranes. Beecher and Adams advocate its use by closed system apparatus (carbon dioxide absorption technic) and report 6.1 per cent pulmonary complications.[1]

Infiltration of procaine hydrochloride and nerve block have the disadvantage that few patients escape without considerable shock and pain. The operation is prolonged and tissue resistance may be reduced, fostering wound infection. A spinal anesthetic has been successfully used by Ackman [2] with relatively low mortality and few complications; however, the hazard of this anesthetic bears less relationship to the condition of the patient, and it still seems that the margin of safety is low.

To have the patient under general anesthesia is desirable. Nitrous oxide, cyclopropane and ethylene are now most widely used. Each of these anesthetics has certain advantages and in selected cases may be preferred. We used procaine hydrochloride and the inhalation anesthetics in our work before 1935. However, we have come to use, more than any other, pentothal sodium without procaine, according to the following method:

TECHNIC

One and one-half grains (0.1 Gm.) of phenobarbital is given the night before operation. A light breakfast is frequently served two or three hours before the operation. One-eighth to ⅙ grain (0.008 to 0.01 Gm.) of morphine is administered. We do not use preoperative barbiturates because we feel that the more rapidly eliminated pentothal sodium works as well without them and that the postoperative recovery time may be delayed by them. Position and preparation of the patient is completed before the injection of 5 per cent pentothal sodium into the cubital vein is started. Blood pressures are checked. Two to 4 cc. of pentothal sodium is given, then a pause of sixty seconds or more permits the anesthetist to judge the patient's sensitivity. Usually 8 or 10 cc. is injected before the operation is begun, then 0.25 to 1 cc. a minute is given during the remainder of the operation as the patient's condition indicates. The deepest anesthesia is often needed at the beginning of the operation to control the reaction to the cutaneous incision. The amount of anesthetic necessary to prevent coughing is usually about the amount needed to prevent movement of the patient and to maintain satisfactory anesthesia. Because of the patient's position constant vigilance is necessary to maintain a free airway. Rarely is a pharyngeal airway required, but an attendant at the patient's head is desirable to maintain the position of the head and jaw. Oxygen is administered by nasal catheter if cyanosis appears, about half the cases requiring oxygen during the anesthetic. Seldom has nikethamide or metrazol been used, but a positive pressure apparatus should be available and has been useful on a few occasions. Administration of the anesthetic is discontinued five to ten minutes before completion of the cutaneous sutures, and the patient frequently moves on the table with the last sutures. The patient is placed on the operated side with a pillow under his head as he is returned to his bed. Intranasal oxygen is administered until the patient is sufficiently aroused to insure full respiratory movements. The patient is turned every few hours to encourage bronchial drainage. One thousand cc. of 5 per cent dextrose and 500 cc. of blood are administered in practically every instance. More intravenous fluids are not necessary in the majority of instances, since patients are rarely more than slightly nauseated for a brief period and fluid intake by mouth is adequate.

RESULTS

One hundred and twenty-three thoracoplasties performed on 53 patients with the removal of from two to six ribs have been reviewed in which the anesthetic agent was pentothal sodium. There were no operative deaths. The average duration of the operation was forty-nine minutes, the longest being one hundred and fifteen minutes and the shortest twenty minutes. The average amount of pentothal sodium used was 24 cc. Only 1 case required more than 40 cc., 50 cc. having been used in this instance.

Some degree of cyanosis was occasionally seen during the early stages of operation associated with light anesthesia, and sometimes breath holding or coughing, but this was always easily controlled by increasing the depth of anesthesia. Postoperative nausea was less than that noted following inhalation anesthetics; 5 patients had rather severe nausea, 45 had very slight nausea and 66 had none. It was thought that in many instances the nausea was due to the opiate rather than to the pentothal sodium.

Four patients had postoperative shock of rather severe degree, and minor degrees of shock were noted in several patients, but the impression gained in observing the patient's condition as he comes out of the anesthesia is that there is less tendency to the symptoms of falling blood pressure, rapid pulse and shortness of breath than is seen in the course of these operations following other anesthetics. The patient's awakening is gradual and not unpleasant, and there is less need for morphine to control pain during the first few hours.

One patient showed some necrosis around the cubital vein from extravasated penthothal sodium solution, and one experienced postoperative mental excitement with disorientation lasting several hours.

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2. Ackman, Douglas: Results of Thoracoplasty in Advanced Pulmonary Tuberculosis, Canad. M. A. J. **45:** 422-425 (Nov.) 1941.

In 2 cases in which expectoration was profuse from empyema with bronchial fistula, pentothal sodium was found to be disadvantageous. Immediately after the pleura was opened the respirations became difficult, and it was necessary to aspirate mucus and pus from the pharynx and hurry the operation. As soon as the empyema pocket was emptied of pus, the patient's condition became less precarious. These patients might have done better under infiltration of procaine hydrochloride.

Roentgenograms were made after most of the stages of the operation, and immediately whenever early symptoms of dyspnea or pain in the chest plus physical signs indicated a possible atelectasis or any other complication.

There is apparently reduced incidence of postoperative spread, only 3 cases being noted in which spread of tuberculosis occurred within two months.

Atelectasis of a lobe occurred in 2 cases. In these 2 cases the atelectasis was on the same side as the operative procedure. In both cases the lung was found to be clear at the end of one month. There was 1 case of postoperative pneumonia which turned out to be spread of tuberculosis and left extensive residual disease in both lower lobes.

The incidence of postoperative atelectasis following a general operation under various types of anesthesia is given variously as follows: by Frias and Fernandez [3] 3 per cent in 556 cases, by Clegg [4] 2.14 per cent in 653 cases, by Eliason and McLaughlin [5] 0.36 per cent in 8,864 cases, by Rovenstine and Taylor [6] 0.44 per cent in 7,874 cases and by Hand and Sise [7] 1.11 per cent in 180 cases. In thoracic surgery, Brunn and Brill [8] report atelectasis in 4.82 per cent in 456 surgical cases and Berry [9] 2.12 per cent in 188 cases. The percentage of atelectasis in our series was 1.7.

REPORT OF CASES

CASE 1.—*Atelectasis.* C. F., a white man aged 27, height 5 feet 9 inches (175 cm.), weight 135 pounds (61 Kg.), had a history of tuberculosis for one year before operation. The amount of expectoration daily was 45 cc. There was moderate dyspnea with apparently asthma-like attacks. Physical examination revealed a fair general condition; preoperative x-ray examinations showed a cavity of moderate size in the central portion of the upper left lobe with considerable infiltration throughout the lobe. The lower lung was clear except for a few minimal small discrete shadows. A left phrenicotomy, five and a half months before, had resulted in moderate elevation of the diaphragm and fixation. Thirteen cc. of pentothal sodium was administered before the operation was started, and a total of 24 cc. was used. The pulse remained between 80 and 90 during the operation. There were 26 inches of ribs removed. The temperature rose to 103.6 F. the second postoperative day; the x-ray examination showed complete opacity of the left lung with displacement of the heart toward the left. Attempted aspiration failed to yield any fluid. One month later the lower part of the lung was found to be clear. Fixation of the left diaphragm undoubtedly favored production of the atelectasis.

CASE 2.—*Atelectasis.* R. F., a white man aged 38, had had tuberculosis for seven years. Expectoration amounted to 60 cc. daily and was positive for tubercle bacilli. There was a cavity 2 inches in diameter in the upper part of the left lung. Following removal of four ribs in the second stage of the operation atelectasis of the lower lobe on the left side developed, which cleared up in one month, and exceptionally rapid closure of the cavity was obtained, and the patient was back at work in six months. The patient has been well two years.

CASE 3.—*Pneumonia followed by spread.* B. S., a Negro woman aged 42, expectorated 30 cc. of sputum daily; she had a cavity in the upper left lobe 3 inches in diameter. Removal of four ribs, 16 inches, in the first stage was followed by pneumonic consolidation of both lower lobes. Two months later x-ray examination showed partial clearing but extensive tuberculous shadows.

Of some interest in assessing the value of the anesthetic may be the late postoperative results. These, however, are so dependent on the classification of the patient's condition prior to operation that for purposes of comparison similar criteria must be utilized. Following the National Tuberculosis Association classification, all but 1 of the 53 patients were in the far advanced stage. Twenty-eight were classed as bilateral, 8 of whom had collapse therapy of the lung contralateral to thoracoplasty. Seven had tuberculous empyema. Of those operated on more than six months ago, 50 per cent have arrested or apparently arrested tuberculosis. The condition in 16 per cent is quiescent, and that in 18 per cent is classified as unstable, in half of which there is improvement. Fifteen per cent of the patients have died, 2 patients within two months. Of these 2, 1 died of wound infection and the other, a very poor surgical risk, of reduced vital capacity and insufficient cardiac reserve. Five died in from one to six years.

COMMENT

Certain attributes are desired in an anesthetic for thoracoplasty. First, the anesthetic must be nonirritating to the respiratory tissue. We have found that patients coming out of the anesthetic following pentothal sodium have no hypersecretion, and there is no change in the character of the sputum.

With other types of anesthesia patients usually go through a period of excitement during which secretions may be dislodged and coughing may be troublesome. During surgery, hyperventilation of the lung with excessive mobility is to be avoided. This is accomplished better with pentothal sodium than with any other anesthetic. In fact, the depression of respiration is apparently an advantage in that it prevents dislodgment of purulent material which may be present under the operative site.

To attempt to give any anesthetic so lightly that the cough reflex is not abolished is unsatisfactory because the half hearted attempts of the patient to free himself of sputum when semiconscious may do more harm than good.

Electrocoagulation is found very useful in accomplishing hemostasis. Failure to dry the wound carefully before final closure delays wound healing and makes for a greater chance of the wound breaking down

3. Frias, E., and Fernandez, F.: Postoperative Platelike Atelectasis, Anesth. & Analg. **19**: 98-101 (March-April) 1940.

4. Clegg, C. G.: Postoperative Atelectasis, U. S. Naval M. Bull. **38**: 531-538 (Oct.) 1940.

5. Eliason, E. L., and McLaughlin, C. W., Jr.: Postoperative Pulmonary Atelectasis, S. Clin. North America **14**: 1-12 (Feb.) 1934.

6. Rovenstine, E. A., and Taylor, I. B.: Postoperative Respiratory Complications: Occurrence Following 7,874 Anesthetics, Am. J. M. Sc. **191**: 807-819 (June) 1936.

7. Hand, L. V., and Sise, L. F.: Nupercaine Anesthesia, Surg. Gynec. & Obst. **71**: 9-21 (July) 1940.

8. Brunn, H., and Brill, S.: Observations on Postoperative Pulmonary Atelectasis, Ann. Surg. **92**: 801-833 (Nov.) 1930.

9. Berry, F. B.: Massive Atelectasis Complicating Paravertebral Thoracoplasty for Pulmonary Tuberculosis, Arch. Surg. **18**: 257-270 (Jan., pt. 2) 1929.

and becoming infected. Several minutes may be cut from the operating time by using electrocoagulation.

Several minutes may also be saved in the induction of anesthesia since pentothal sodium provides surgical anesthesia within two or three minutes after it is started.

The absence of postoperative nausea constitutes an advantage which we consider extremely important in combating the discomfort and shock of the operative procedure. It is hardly necessary to point out that if one starves a normal, healthy person for twenty-four hours considerable weakness results. If this is added to the effects of the operation, delayed recovery is to be expected. With pentothal sodium, a small breakfast given two or three hours before operation seems perfectly safe, and many patients eat solid food within two hours after the operation, and most of them eat the regular evening meal. Patients' spirits are correspondingly good the evening of the operation.

Awakening from this anesthetic is more like awakening from a night's sleep than from an artificially imposed anesthesia, and when operative procedures require repetition—sometimes five or six stages—the patient's morale is less likely to be destroyed than with an unpleasant anesthetic experience.

We believe that pentothal sodium is to be recommended for thoracoplasty.

1005 Professional Building.

Clinical Notes, Suggestions and New Instruments

NEUROFIBROMA (NEURINOMA) OF THE FOOT

EMIL D. W. HAUSER, M.D., CHICAGO

An 11 year old girl was brought in Aug. 2, 1939 because of pain in the ball of the right foot, which had been present for six months. The family physician had taken roentgenograms, which were negative, and he was of the opinion that she had a calcified bursa on the plantar surface of the foot. With no improvement after six months the parents consulted another physician, who referred her to me. She gave a history of having had pyelitis, and on getting up after prolonged bed rest the foot was painful. She also had had some callus form under the anterior arch, which had since disappeared. There was some pain in the region of the longitudinal arch.

Examination showed a definite tumor on the plantar surface of the foot, which was very tender. This tumor was beneath the shaft of the first metatarsal bone and was felt to be about the size of a bean. The possibility that this might be a ganglion was considered. She also had a slight valgus deformity and a slight lowering of the arch of the right foot. It was thought that she had some foot strain with beginning pes valgoplanus. The foot strain was relieved by means of adhesive strapping, but the pain and swelling beneath the head of the first metatarsal bone did not subside. Surgery was advised. The possibility that this might be a glomus tumor, neuroma, fibroma, ganglion and inflammation of the bursa with calcification was considered.

Under ethylene anesthesia the tumor was exposed and a small, encapsulated tumor, about ½ inch in diameter, was removed. It was found to be attached to the plantar fascia. The tumor contained a thick mucinous-like material. At the time of operation it had the appearance of a small ganglion. The report of Dr. Donald O. Manshardt, pathologist, stated that the tumor consisted of irregular shaped, firm, cauliflower-like, white tissue. Intermingled strands of what appeared to be adult connective tissue were found in these sections. In places these were in poorly formed whorls, in which there was some suggestion of palisading of nuclei. Rarely there was definite palisading. There was also some hyalinized connective tissue which divided this more cellular tissue into capsules or poorly defined bundles. About the periphery of these areas there were smaller clusters of cells, arranged in whorls, which superficially resembled the psammomatous type of meningioma except that there was no calcification. These whorls occurred in long, channel-like formation, composed of interlobular connective tissue. The entire structure resembled nerve in its architectural configuration. No normal nervous elements were seen.

The diagnosis was made of a large neurinoma from the plantar region of the right foot. (Note: The term "neurinoma" avoids the implications as to the origin of the tumor cells suggested by "neurofibroma" or schwannoma.) The wound

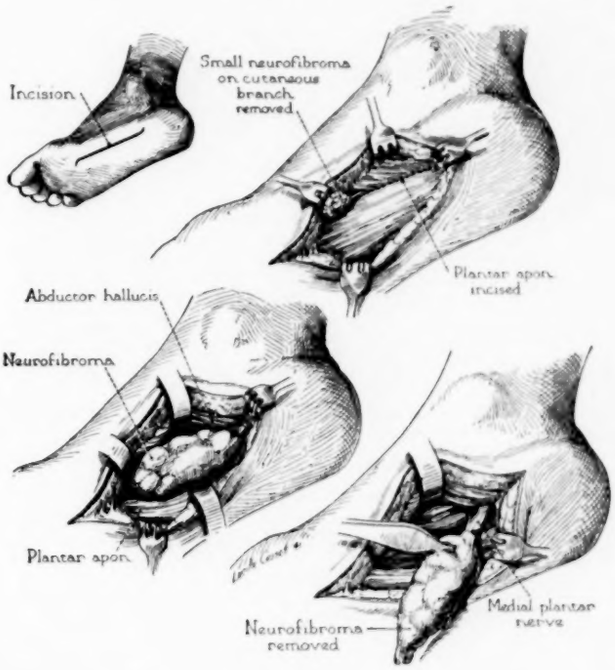

Fig. 1.—Operation for neurofibroma of the foot.

healed without any difficulty, and pads were placed in the shoes to avert any further development of foot strain. The child stayed free from symptoms until six months later, when she again noticed pain and tenderness underneath the arch of the right foot.

The pain increased, so that on June 7, 1941 she returned for examination. At this time the slightest pressure over the plantar surface beneath the navicular bone caused intense pain. There was a definite fulness in this area, which was visible and palpable.

In view of the fact that previously a neurofibroma had been removed from this foot, it was thought that a similar tumor might have occurred higher along the nerve. She entered the hospital on June 11, 1941 for operation. A longitudinal plantar incision was made and a small area of fibrous tissue was found where the previous tumor had been removed (fig. 1). The plantar fascia was distended and a tumor could be felt beneath it. The plantar fascia was incised, and a large tumor the shape of a sausage was exposed. It consisted of a lobulated soft mass which was well encapsulated. The tumor was easily dissected from the tendon sheaths in the area and was traced up until it ended in the deep plantar nerve. Normal nerve

tissue was seen to end where the tumor started. The plantar fascia and skin were closed. Convalescence was uneventful and the patient left the hospital in about twelve days. There was a slight amount of paresthesia in the area of the operation.

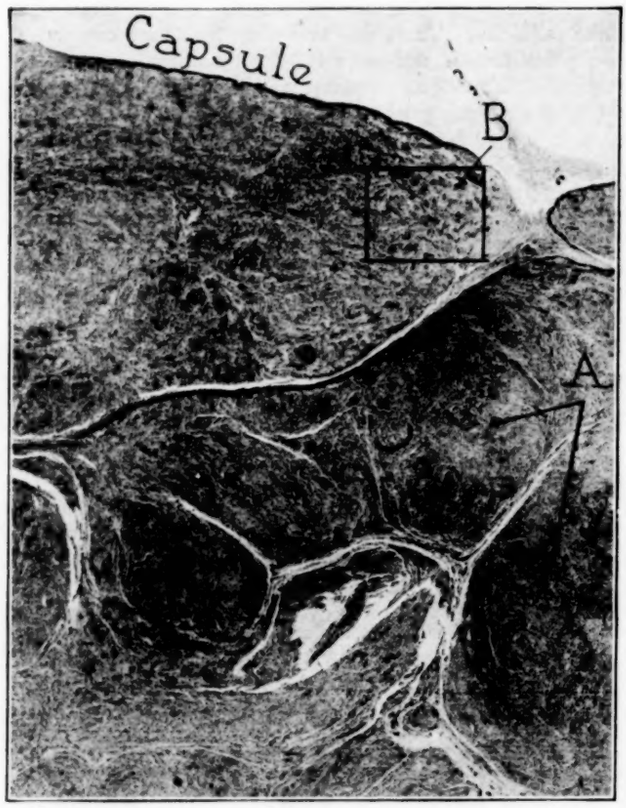

Fig. 2.—Low power section of tumor stained with hematoxylin and eosin: *A*, large whorls; *B*, section taken for figure 3.

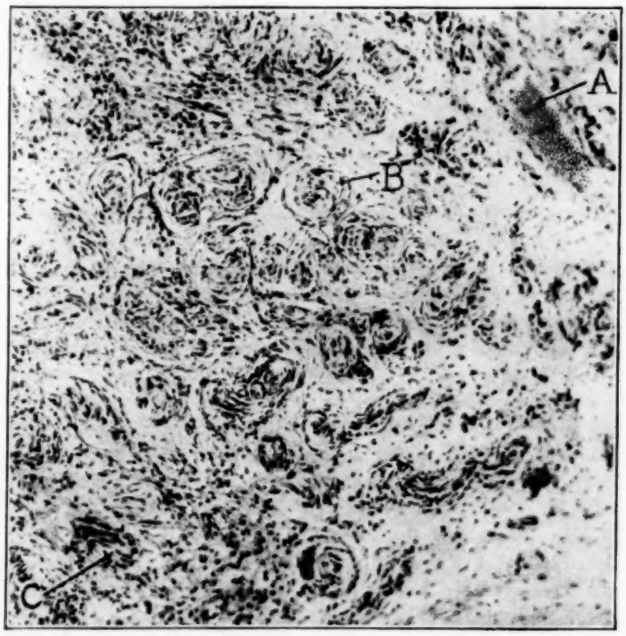

Fig. 3.—Section slightly reduced from a photomicrograph with a magnification of 85 diameters, stained with hematoxylin and eosin: *A*, blood vessel; *B*, proliferation about nerve axons; *C*, palisades of nuclei.

Dr. Manshardt's report on the specimen stated that the tumor was a large, elongated, firm, encapsulated, pearly white mass whose external surface was loosely lobulated and irregular (figs. 2, 3 and 4). The mass measured 6.5 by 2 cm. On the cut surface there were numerous circumscribed gray-white whorls of tissue. Two blocks, six sections, were made. The first block was of a well encapsulated, lobulated mass of tissue composed of cells having large, vesicular, elongated nuclei of oval or spindle shape. These were arranged in large concentric whorls with rather abundant mucoid intercellular substance. The cells were rather uniform in appearance throughout the section. In some regions small concentric whorls were seen, but for the most part the tumor cells were rather loosely arranged, showing a slight tendency toward palisading of the nuclei. There were no areas of increased density, increase in mitotic figures or invasion of the capsule to indicate that the tumor might be malignant.

Sections stained with van Gieson's stain showed the presence of a moderate amount of collagen in the tumor. Davenport's nerve fiber stain revealed the presence of occasional nerve fibers. In the area pictured in figure 3 (magnified 85 times) a nerve

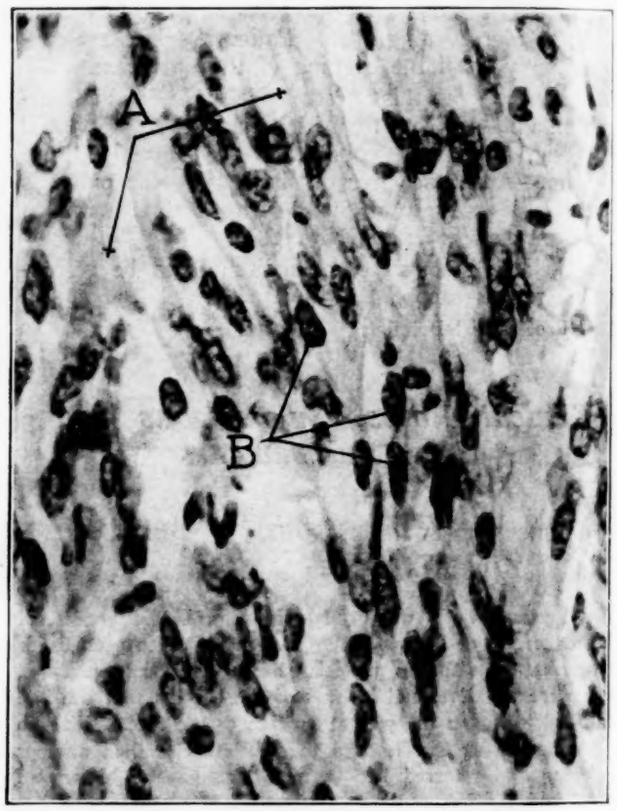

Fig. 4.—Section magnified 660 times, stained with hematoxylin and eosin: *A*, mucinous intercellular substance; *B*, neurinoma cells.

fiber is found at the center of each of the small whorls, surrounded by concentric layers of cells. Diagnosis was made of a large neurinoma from the plantar area of the right foot. Ewing [1] states that this type of tumor affects mainly the larger nerve trunks and occurs in nearly all parts of the body, forming encapsulated, slowly growing, firm or soft masses attached to the nerve trunk. They have a definite tendency to recur locally from remaining tumor tissue if not completely removed and may become malignant and locally invasive following recurrence. It is rather common to find a new tumor develop higher up in the nerve trunk. This may be the result of a new growth or extension of the original tumor cells within the epineurium.

A neurofibroma of the deep plantar nerve is a rare tumor. Neurofibromas have been reported in many nerves of the body, and it is not unusual to have recurrences in the nerve proximal to the original tumor, as was seen in this case. The possibility of another recurrence higher up with more serious complica-

1. Ewing, James: Neoplastic Diseases; Treatise on Tumors, ed. 4, Philadelphia, W. B. Saunders Company, 1940.

tions must still be kept in mind. The patient has been kept under observation for two and one-half years after the second operation and has shown no sign or symptom of recurrence, so that the possibility of recurrence has become quite remote.

8 South Michigan Avenue.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT. HOWARD A. CARTER, Secretary.

E & J RESUSCITATOR, INHALATOR, ASPIRATOR (FOX MODEL) ACCEPTABLE

Manufacturer: E & J Manufacturing Company, 139-141 South Verdugo Road, Glendale, Calif.

The E & J Resuscitator, Inhalator and Aspirator, Fox Model, is designed to be used in emergencies in which natural respiration has failed with resulting asphyxia. It is similar in operation to the E & J Resuscitator and Inhalator which was accepted by the Council (THE JOURNAL, May 13, 1939) for use only by professional or other adequately trained personnel. In construction the Fox Model is different from the earlier one in that a venturi is used in place of the piston to create the suction; it is available in portable and hospital models.

In the Council's investigation of the apparatus it was found that the unit was sturdy in construction and appeared to be capable of withstanding ordinary wear and tear. There are yokes to accommodate two high pressure oxygen cylinders, or cylinders of mixed gases (sizes A to E). A pressure gage which registers the approximate pressure of gas in the open cylinder serves to warn when the cylinder is becoming depleted.

Mechanically, the E & J Resuscitator, Inhalator and Aspirator, Fox Model, utilizes gas pressure in the cylinder to control delivery of (1) alternating positive and negative pressure through two tubes to the face mask, (2) constant flow of oxygen (or any gas mixture) to the face mask and (3) negative pressure said to be equal to 16 ounces per square inch, available in a separate tube designed to suck mucus from the air passages to a trap bottle furnished with the apparatus. Three positions of a lever determine which one of these three functions is in action at a given time. No two can be available simultaneously. The intricate mechanism which secures negative pressure for suction and for the expiratory phase of artificial respiration apparently is operated on the so-called Venturi principle, after the fashion of the steam injector or a Chapman vacuum pump. The manufacturer claims that positive pressure of 13 mm. of mercury and 9 mm. of mercury negative pressure is delivered to the mask alternately. Experiments with the model submitted have verified this claim to be substantially correct. Variations did not exceed 2 or 3 mm. of mercury under varying conditions in human subjects. Investigations included records made of pressure in the bronchus when no respiratory activity of the human subject was present. These positive and negative pressures are permanently adjusted at the factory and cannot be changed by the operator. The actual negative pressure for suction corresponds to that claimed in the pamphlet. It can be asserted that the apparatus furnishes adequate pulmonary ventilation provided airtight contact of the mask is maintained with a patient whose air passages are unobstructed. The positive and negative safety flow-off valves are set at 18 mm. of mercury.

The masks for an adult and an infant are adequate for the purpose. They are provided with an exit valve which is easily closed tight during use of the machine for artificial respiration and, when opened, acts freely when the lever is in the position for inhalation of oxygen by the patient. An inlet valve at the machine end of the connecting tubing permits inhalation of environmental atmosphere if the supply of gas in the cylinders becomes exhausted during use of the "inhalator."

It is obvious that negative pressure to provide suction of foreign liquids from the respiratory tract is desirable for depressed patients. Two characteristics of such negative pressure are important: (*a*) actual pressure provided; (*b*) the volume of atmosphere moved at this pressure in a given time. To remove vomitus or other fluids quickly and safely the actual negative pressure should be moderate and the volume of atmosphere sucked in a given time should be maximal.

It can be stated that the Fox Model E & J Resuscitator does what is claimed for it; namely, it maintains adequate pulmonary ventilation when properly used. The term "Properly used" means that the mask is kept in airtight contact with the face and that the air passages are free of obstruction.

The evidence that has been made available indicates quite clearly that the machine has demonstrated its worth in trained hands. The critical data consisted of many reports on the use of the resuscitator in the fields of surgery and obstetrics.

It must be pointed out, however, that the process of blowing oxygen into the lungs and aspirating it has a reverse effect on the circulation from that of normal respiration. Normal respiration tends to facilitate the exchange of gases in the lung capillaries. When the lung is inflated, even at very moderate pressures, circulation through the lung capillaries is retarded for an instant, since the blood pressure in these capillaries is very small. Stoppage here necessarily affects the entire circulation. However, periodic stops last only a moment, since the peak pressure (14 mm. of mercury) is maintained for only a short part of the cycle.

E & J Resuscitator, Hospital Model.

Another point should be borne in mind: While artificial respiration has been maintained by systems of this type in physiologic laboratories where experiments are performed on animals with the chest opened, the pressure required for adequate ventilation in such cases is much less than that required to distend the lung when the diaphragm must be forced down against the pressure of the abdominal contents and the bony thorax distended by pressure exerted by the lung from within.

In accepting the apparatus, the Council wishes to stress two points: (*a*) No artificial resuscitator or inhalator should replace the training of medical men and first aid men in the prone pressure method of resuscitation; (*b*) it is very important that this machine be used by well trained operators who have received their instruction from competent physicians.

The acceptance of this apparatus, therefore, is not to be regarded as a recommendation to abandon prone pressure methods of artificial respiration. In cases needing resuscitation, the prone pressure method should be instituted immediately pending the arrival of any type of resuscitator, inhalator or respirator, provided the patient's condition permits.

It is manifestly impossible to apply prone pressure artificial respiration in all conditions which arise in medical practice, as instanced in surgical operation on the abdomen when respiration fails. In such cases a mechanical resuscitator device for maintaining artificial respiration over short periods may be very desirable. Operators who are trained to use the mechanical resuscitator should also be equally well trained in the prone pressure method of artificial respiration.

The Council on Physical Therapy voted to accept the E & J Resuscitator, Inhalator, Aspirator, Fox Model, for inclusion in its list of accepted apparatus, with an understanding of the limitations and hazards of positive pressure resuscitators, with the expectation that it will be used only by professional or other adequately trained personnel.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, APRIL 10, 1943

FURTHER EXPERIMENTAL STUDIES OF BLAST INJURIES

The basic experiments of Hooker and of Zuckerman demonstrated that the effects on the body of explosions both in air and in water are primarily due to the externally applied pressure wave. Williams [1] observed that pressures set up by an explosion at some depth in water create a new factor. When the pressure wave reaches the surface, transmission of the pulse to air does not occur but there is reflection as a wave of tension at an angle equal to the angle of incidence. The human body, according to Williams, has roughly the same density as water. When the pressure wave impinges on the body reflection does not follow but the pulse will be transmitted through the tissues without displacement just as if the body were so much water. However, when the transmitted pulse encounters an air cavity in the body as, for example, the lungs, the static wave of pressure will change into a wave of kinetic energy in the layers of tissues lining that cavity and a disruptive effect will occur. Hence the lungs and other gas filled cavities in the body are particularly susceptible to damage from the pressure wave even though the body itself may not be deeply immersed.

Greaves and his associates [2] exposed rats and guinea pigs to explosions of tetryl (dinitrophenylmethylnitramine) in a welded steel tank 70 by 48 by 42 inches filled with water. The charge was detonated 20 inches below the surface while the animals were swimming within a 2 foot circle beyond the point directly over the charge. Goats were exposed to the effects of a 300 pound depth charge exploded 50 feet below the surface in water 100 feet in depth. Lethal, sublethal and minimum lesions were induced and studied. The lesions in the lungs included diffuse hemorrhage throughout the entire parenchyma. Microscopic studies of these lesions revealed that the first evidence of injury was rupture of the capillaries and hemorrhage into the interalveolar septum. Similar observations were reported by Cameron, Short and Wakeley.[3] Two types of lesions were seen in the gastrointestinal tract in the lethal cases: hemorrhagic discolorations of the bowel wall and perforations. Both types were definitely related to the presence of gas within the lumen. When 20 cc. of air was injected into the peritoneal cavity of a rat which was then subjected to a lethal underwater blast, laceration of the liver and spleen and extensive hemorrhage into the abdominal wall resulted. Injuries of these structures were not seen when normal animals were blasted. Four short segments of normal rabbit intestine were removed and ligated at both ends after the first was completely collapsed, the second filled with air, the third with isotonic solution of sodium chloride and the fourth with air and saline solution. They were then submerged and subjected to underwater blast. The collapsed segment and the one filled with saline solution were unaffected but the two containing air were ruptured. These investigators also found that kapok and foam rubber are best capable of preventing or minimizing the injurious effects of the compression wave in the experimental animals.

Both clinical and experimental evidence has established that immersion blast produces abdominal trauma in addition to the chest lesions seen in air blast. Friedell and Ecklund [4] were particularly interested in factors which lead to the production of intestinal perforation. They attempted to determine by animal experiments whether the perforations occurred immediately or were the delayed effect of severe intestinal trauma. Reports of hemorrhagic areas in the bowel following blast injury created the impression that the hemorrhage was followed by necrosis of the wall with perforation and peritonitis. Experiments were performed in a large steel tank measuring 8 by 6 feet filled with water to a depth of 4 feet. Postmortems on guinea pigs which died immediately or shortly after exposure in a water filled tank to a blast caused by detonating caps containing a charge of 35 grains of fulminate of mercury revealed that the abdominal wall was uninjured but that there were areas of subserous hemorrhages over the colon and small bowel and especially over the enlarged appendix. Most serious changes were noted over fecal collections. The lungs had symmetrical hemorrhagic areas. Microscopic studies did not reveal perforations of the intestinal tract. Abdominal lesions were not pro-

1. Williams, E. R. P.: Blast Effects in Warfare, Brit. J. Surg. **30**: 38 (July) 1942.

2. Greaves, F. C.; Draeger, R. H.; Brines, O. A.; Shaver, J. S., and Corey, E. L.: An Experimental Study of Underwater Concussion, U. S. Nav. M. Bull. **41**: 339 (March) 1943.

3. Cameron, G. R.; Short, R. H. D., and Wakeley, C. P. G.: Pathological Changes Produced in Animals by Depth Charges, Brit. J. Surg. **30**: 49 (July) 1942.

4. Friedell, M. T., and Ecklund, A. M.: Experimental Immersion Blast Injury, U. S. Nav. M. Bull. **41**: 353 (March) 1943.

duced except when the lungs were so severely damaged that death ensued. To eliminate the severe lung injury these investigators devised a chamber which minimizes the effects of blast on the thorax. With this chamber the lungs were protected so that previously fatal explosive conditions were no longer lethal. The abdominal lesions were present, however, and as the force of the charge seemed to grow greater the hemorrhagic lesions gave way to perforations.

In the cases observed by these authors at the hospital it was felt that possibly the life jacket prevented such severe injuries to the lungs as to cause death and that the abdomen, which was unprotected, bore the brunt of the explosion. This seems to be borne out by their experiments in which the previous lethal condition was repeated except that the chest was protected. Perforations were then found in the intestinal tract, and the animal survived the immediate explosion. They therefore conclude that the perforations are an immediate result of the blast and do not occur later as a result of necrosis of the bowel wall. These perforations therefore demand early surgical intervention; hemorrhagic lesions do not require surgical treatment. It is suggested that extension of the life jacket to cover the abdomen would be beneficial. The authors did not find evidence in their experiments that water was forced through the anus with rupture of the bowel. The lesions seemed to be a direct effect of the explosive force transmitted through the elastic walls of the abdomen and thorax.

Observations on the occurrence of intracranial trauma following blast injury are few. Unfortunately Wilson and Tunbridge [5] did not have opportunity to examine the brain and spinal cord in their necropsies on 12 persons who died as a result of blast injury. In Ascroft's [6] fatal case of multiple injuries due to the explosion of a hand grenade at short range, in addition to the extensive infiltration of the lungs, a peculiar discoloration of large areas of the cerebral hemispheres was found as the result of the great numbers of minute hemorrhages confined to the gray matter of the cortex. This observation seems to be unique. The lesion did not resemble any hitherto described as following death from blast. Zuckerman reported pial hemorrhages on the surface of the cortex and hemorrhages from the tela choroidea, but hemorrhages did not occur in either the gray or the white matter of the brain in monkeys subjected to blast pressures as high as 110 pounds per square inch. Friedell and Acklund did not note hemorrhages into the brain in their experimental animals which died primarily as a result of a blast. They felt that a blast wave sufficiently forceful to produce intracranial trauma would with certainty cause fatal lesions of the intrathoracic and intraperitoneal structures.

Abbott, Due and Nosik [7] call attention to a small group of patients with a history of exposure to severe concussion, loss of consciousness for a period varying from a few minutes to several days, persistent headaches, memory loss and irritability. Positive neurologic signs are minimal. The most common are a slight facial palsy, a transient hemiparesis and occasionally a transient change in reflexes. There is a history of coma, syncope or convulsions which did not exist prior to the blast and a definite departure from a stable personality. Such patients are often regarded as having a functional disturbance—a psychoneurosis or traumatic neurosis. These authors advance the idea that these symptoms are characteristic of a subdural hematoma or a subdural effusion. Pneumoencephalography will demonstrate a characteristic filling defect over the cerebrum in these cases with a distortion of the ventricular system in some. A trephine opening over the indicated superior temporal area, with incision of the dura, will permit the escape of either old blood or xanthochromic fluid. Of 10 cases in which this procedure was performed, 7 resulted in subdural effusions, 2 were instances of subdural hematoma and 5 were bilateral. There were no operative fatalities. The symptoms were promptly relieved. The last quoted reports suggest that cerebral lesions must be taken into consideration, as possible direct or contributing factors in the mechanism of death in blast injuries and as a cause of certain late complications, such as subdural hematoma and subdural effusion.

Obviously, the difficulty of diagnosis in such obscure conditions should not be increased by a too liberal use of narcotics. Surgeons have suggested that morphine is contraindicated in the acute phase of blast injuries because it tends to accentuate the pulmonary edema and obscures the symptoms of abdominal and cerebral complications. Its use would seem to be justified only in the presence of painful injury or excessive restlessness.

The numerous reports now appearing in medical periodicals and the many unanswered questions that are being raised relative to the effects of blast on various systems in the human body indicate the need for further investigation, both clinical and experimental. The approach through special committees or subcommittees of the Office of Scientific Research and Development and the Division of Medical Sciences of the National Research Council, which has been so successful in other problems, might well be applied in the case of blast.

5. Wilson, J. V., and Tunbridge, R. E.: Pathological Findings in a Series of Blast Injuries, Lancet **1**: 257 (Feb. 27) 1943.

6. Ascroft, P. B.: Blast Injury of the Lungs with a Curious Lesion of the Cerebrum, Lancet **1**: 234 (Feb. 20) 1943.

7. Abbott, W. D.; Due, F. O., and Nosik, W. A.: Subdural Hematoma and Effusion as a Result of Blast Injuries: First Preliminary Report, J. A. M. A. **121**: 664 (Feb. 27) 1943; Second Preliminary Report: Diagnosis by Psychiatric Examinations, ibid. **121**: 739 (March 6) 1943.

Current Comment

PLANS FOR THE WAR BLINDED

Among the casualties of war few merit more immediate consideration than that given to those who become sightless as a result of their participation in the national defense. In World War I, according to available figures, less than 250 Americans were blinded. Thus far the number of British soldiers who have become sightless, including the men from Great Britain and the colonies, is somewhat less than a few hundred. Planning bodies, therefore, estimate that the number of Americans in the armed forces who become totally blind will not exceed a few hundred. For the past six months representatives of the Surgeon Generals of the Army, the Navy and the Public Health Service, the administrator of the Veterans Administration, the Federal Board of Hospitalization and the ophthalmologic committee of the Division of Medical Sciences of the National Research Council have been engaged in a study of the problem. An elaborate program has been developed to rehabilitate socially and economically those who become sightless. Sufficient funds have been provided by the Congress to meet every possible need. The plans contemplate utilization of existing agencies which deal with the blind. However, public fund raising campaigns are unnecessary since the over-all need is hardly sufficient to demand special expansion for this purpose in the services of unofficial agencies. In accordance with the executive order of the President, the social rehabilitation of the blind becomes a function of the Veterans Administration and is to be handled by the Division of Educational Rehabilitation and not the medical division. Through the cooperative effort now in process of development the rehabilitation will begin just as soon as the diagnosis is made and will continue from the time of reception of the invalid by the armed forces until the man can be discharged from the Veterans Administration physically, mentally and socially rehabilitated.

THE DISTINGUISHED SERVICE MEDAL

The Distinguished Service Medal of the American Medical Association will be presented for the sixth time at the meeting on Tuesday night, June 8, in the ballroom of the Palmer House, Chicago, during the regular session of the House of Delegates of the American Medical Association in Chicago, beginning June 7, 1943. The medal was awarded, for the first time, in 1938 to Dr. Rudolph Matas of New Orleans, in 1939 to Dr. James B. Herrick of Chicago, in 1940 to Dr. Chevalier Jackson of Philadelphia, in 1941 to Dr. James Ewing of New York and last year to Dr. Ludvig Hektoen of Chicago. This award is recognized as one of the most distinguished honors within the gift of the American Medical Association. Any Fellow of the Association may submit nominations, which should be sent, together with a record of the scientific services of the nominees, to the chairman of the Committee on Distinguished Service Award, Dr. A. A. Walker, 2250 Highland Avenue, Birmingham, Ala., or to the Secretary of the Association at 535 North Dearborn Street, Chicago. Of all nominations received by the committee, five are submitted to the Board of Trustees of the Association, from which the Board selects three to be submitted to the House of Delegates at its first meeting at the time of its regular session. Immediately on submission of the nominations by the Board of Trustees, the House of Delegates by official vote selects the recipient of the honor, to whom the Distinguished Service Medal is presented at the meeting at which the President-Elect is installed as President, which is usually on Tuesday evening of the week of an annual session. An extended list of distinguished physicians nominated for this award will enable the committee, the Board of Trustees and the House of Delegates, all of whom participate in the selection, to determine for 1943 a recipient of distinction, whose nomination will reflect favorably on himself and on the Association.

LEGAL MEDICINE IN PHILADELPHIA

The coroner of the county of Philadelphia, the first physician to hold the office since 1878, has developed a program that may be expected to increase the efficiency of his office and will in addition contribute materially to the dissemination of knowledge of the subject of legal medicine. In an effort to put the functioning of his office on a scientific, efficient basis he has created an advisory board consisting of the president of the county medical society, the director of legal medicine at Temple University, a professor of sociology who is also an authority on criminology, an associate professor of medicine, and the president of the College of Pharmacy. Special consultants have been named who will be able to bring to the work of the coroner's office specialized knowledge whenever the occasion demands, consultants in toxicology, consultants in ballistics and consultants in medical and legal research. Realizing the potential value for purposes of instruction of the material that passes through his office, the coroner has formulated a plan under which the six medical schools of the city may have access to that material by conducting classes each week in the morgue. A series of lectures on legal medicine under his direction has recently been concluded. The lectures were given in the headquarters of the Philadelphia County Medical Society under the sponsorship of that society, the six medical and two law schools, the bar association, the College of Pharmacy and the office of the district attorney. The lectures were well attended by medical, law, pharmacy and police students and by physicians and lawyers. No admission charge was made. A tentative selection has been made for a similar series to be given in the fall, and plans are being considered to repeat the program annually. In integrating as he is the various groups in the community that should be concerned in the development and dissemination of knowledge of legal medicine and in associating the coroner's office so intimately with that development, Dr. Herbert M. Goddard may well be constructing a pattern that will be followed elsewhere.

MEDICINE AND THE WAR

In this section of The Journal each week will appear official notices by the Committee on War Participation of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medicine and the war and such other information and announcements as will be useful to the medical profession.

ARMY

INTERNS AND RESIDENTS IN AIR FORCE HOSPITALS

Policy to Be Followed in Placing Present Interns and Residents Who Will Be Assigned to the Army Air Forces

Those interns and residents who are ordered to duty with the Army Air Forces are to be given a period of training which will augment the training received in civilian life. The first six months of this training will have a distinct military character and wll be carried out as follows:

1. A policy of indoctrination and assignment of interns and residents entering the Army Air Forces is to be established in specified Army Air Force hospitals.

2. The purpose of this plan is to acquaint the newly assigned officers with army hospital routine and to give them further concentrated professional training. Such placement will materially aid the permanently assigned officers in the Army Air Force hospitals with their routine work.

3. The program will function as follows:

(*a*) Men will be assigned from Carlisle Barracks to designated Army Air Force hospitals by the Air Surgeon at the approximate ratio of 1.5 officers per hundred hospital beds.

(*b*) These officers will serve as junior assistants for a period of approximately six months in the larger hospital installations.

(*c*) These junior officers will be assigned to ward work under a senior officer, preferably one who has had some teaching experience or who is personally adaptable to teaching. He will act as consultant and adviser for the junior officer or officers under him. The junior officer will keep records, make physical examinations and take over all routine work under the direction of his senior officer.

(*d*) The detailed division of training should be approximately as follows:

(1) Routine ward work, five hours daily (example: 0800 to 1200, routine work; 1600 to 1700, afternoon ward rounds).

(2) Drill or physical education, one hour daily.

(3) Lectures on x-ray, laboratory, medical, medical administrative or military subjects, two hours daily. In this period could be included firing on the range and work with field units.

(*e*) Regular staff conferences should be held at specified times covering x-ray, electrocardiography, clinical pathology and general medical and surgical problems.

4. The general division of time in the six months training period for junior officers will be divided approximately as follows and the men should rotate through the entire service whenever possible:

	Per Cent
Medical service	40
Surgical service	20
Dispensary service	10
Eye, ear, nose and throat service	10
X-ray service	10
Venereal disease control and immunization	10

5. Junior officers will be graded weekly by their consultants and at the end of a six months period a final grade will be given to each junior officer by the post surgeon. Professional ability, adaptability to army routine and qualities of leadership will be considered in the final evaluation. Military necessities permitting, the upper third of the class will be allowed to choose between a second period of six months in a preferred straight residency in the same hospital installation or of being assigned to the School of Aviation Medicine, preference of service being given in the order of class rank. The remaining members of the class will then be assigned, by the Air Surgeon, to smaller hospitals serving the flying fields, in order that they may gain some first hand knowledge of this type of service. After an additional period of service at this type of installation they will be further classified for the School of Aviation Medicine or a general duty assignment. Residents whose civilian training has been interrupted will when possible continue training in that specialty.

6. This program is designed to mature the younger medical officers more quickly and to utilize their efforts in the best way possible from the onset of their assignment. Such utilization, under supervision, will relieve the senior officers from much of their routine work and release them for more important professional duties. The junior officers thus assigned should profit tremendously by the experience and personal guidance of their seniors.

TRAINING FOR FIELD WORK

Three hundred and twenty-two more officers of the Medical Department qualified on March 11 for duty with medical units in the field when they were graduated from the Medical Field Service School at Carlisle Barracks, Pennsylvania. The officers completed six weeks of grueling training. These experienced physicians, dentists and sanitary engineers left immediately after the exercises for their respective units. The training course here in medical field work taught them the military knowledge necessary for them to be efficient Medical Department officers, capable of carrying out medical preventive measures and caring for the sick and injured under war conditions. The subjects taught included training, medical support, tactics, military sanitation, logistics, field medicine and surgery, and administration, presented in an intensive six weeks program of daily lectures, home study and field demonstrations.

AT A JUNGLE FIRST AID STATION IN PANAMA

An army doctor at a jungle outpost in the Panama Canal Department is a military tactician as well as a physician, as with his help it is possible to maintain gun and searchlight positions in the jungle. The officers and enlisted men of the medical department have hacked their way through the jungle, built first aid stations and are largely responsible for the lowest malaria rate in the history of the Army in Panama. Ambulances can now reach many of these positions to bring in soldiers requiring hospitalization, while formerly litter bearers had to carry a sick man for miles. Army doctors attached to one Coast Artillery unit still must travel 225 miles a day to cover a few of the emplacements in the jungle. These officers daily look for mosquito breeding places. Continuously they move first aid stations into different positions in the jungle. A first aid station which can be packed into two trunks is built near emplacements. Emergency operations can be performed at a moment's notice in these aid stations. One jungle position for over a year has had a perfect sanitation record, and not one man has had malaria. Occasionally natives living in the jungle call at first aid stations to be treated. The dentists who visit the emplacements regularly carry their equipment in a trunk containing a folding steel chair, foot engine and surgical dental equipment. The biggest problem confronting the jungle medical detachment now is transportation. The positions are so scattered that much time is taken up by traveling.

THE VALLEY FORGE GENERAL HOSPITAL

One hundred and sixty-five years after General Washington made his famous encampment at Valley Forge, the new U. S. Army Valley Forge General Hospital was officially opened, February 22, at Phoenixville, Pa., which is only a short distance from the historic region. This vast army hospital has a capacity of about 2,000 beds in two story brick structures connected by hallways. The commanding officer of the Valley Forge General Hospital is Col. Henry Beeuwkes of Jamesburg, N. J., honor graduate of the Army Medical School in the class of 1909 and personal physician to General Pershing during the first world war. Colonel Beeuwkes later resigned his commission in the Army to become associated with the International Health Board of the Rockefeller Foundation and for many years carried on research in yellow fever for that organization in Africa. The administrative work of the Valley Forge General Hospital is carried on by twenty-three medical administrative, quartermaster, engineer and finance officers.

As of March 15, the professional staffs of the hospital were as follows:

EXECUTIVE AND ADMINISTRATIVE SERVICE

Col. Henry Beeuwkes, commanding officer.
Lieut. Col. Robert D. Smith, executive officer.
Major Alfred G. Gillis, director of medical training.
Major Arthur Heyman, director of dietetics.
Major Bernard M. Murphy, receiving and disposition officer.

MEDICAL SERVICE

Lieut. Col. Marshall N. Fulton, chief of medical service.
Major Maurice A. Schnitker, assistant chief of medical service and chief of general medical service.
Major Seymour Fisher, station surgeon and outpatient service.
Major Samuel Morrison, chief of gastrointestinal section.
Capt. Louis K. Alpert, chief of cardiovascular-renal section.
Capt. Michael J. Lepore, chief of officers and women section.
Capt. Raymond J. Rickloff, chief of communicable disease section and consultant in dermatology.
Capt. Russel W. Lyster, assistant chief of general medical section.
Capt. Paul N. Morrow, assistant chief of communicable disease section.
1st Lieut. Loren F. Blaney, ward officer, cardiovascular-renal section.
1st Lieut. Allen S. Cross, ward officer, officers and women section.
1st Lieut. Elliot D. Giddon, ward officer, general medical section.
1st Lieut. William G. Layton, ward officer, communicable disease section.
1st Lieut. Dean Rizer, ward officer, cardiovascular-renal section.
1st Lieut. Robert E. Westmoreland, ward officer, gastrointestinal section.

SURGICAL SERVICE

Lieut. Col. Ralph J. Haws, chief of surgical service.
Major Charles M. Robbins, assistant chief of surgical service and chief of general surgical section.
Major Spencer T. Snedecor, chief of orthopedic section.
Major Irvin S. Koll, chief of urologic section.
Major Charles W. Boyd, chief of eye, ear, nose and throat section.
Capt. Albert J. Abbot, ward officer, eye, ear, nose and throat section.
Capt. John M. Borbonus, chief of officer and women section.
Capt. Merian Gearhart, ward officer, general surgical section.
Capt. Philip E. Lear, ward officer, general surgical section.
Capt. Charles D. Lenhoff, ward officer, urologic section.
Capt. Willis H. McKean, ward officer, general surgical section.
Capt. Phillip J. Morgan, ward officer, general surgical section.
1st Lieut. Francis L. Coffey, ward officer, orthopedic section.
1st Lieut. Walter C. Graham, ward officer, orthopedic section.
1st Lieut. Clinton A. Hays, chief of septic surgery.
1st Lieut. George E. Lowery, chief of physical therapy.
1st Lieut. Stephen M. McCoy, ward officer, officer and women section.
1st Lieut. Karl S. Russell, chief of operating and anesthesia section.

NEUROPSYCHIATRIC SERVICE

Capt. Walter E. Barton, chief of neuropsychiatric service.
1st Lieut. Dallas Pratt, ward officer, neuropsychiatric service.
1st Lieut. Daniel S. Jaffe, ward officer, neuropsychiatric service.

X-RAY SERVICE

Capt. John Francis Miller, chief of x-ray service.
1st Lieut. Edward H. Gregman, assistant chief of x-ray service.

LABORATORY SERVICE

1st Lieut. Hans G. Schlumberger, chief of laboratory service.
1st Lieut. Robert D. Johnston, assistant chief of laboratory service.
2d Lieut. Edmund P. Finch, laboratory service.

DENTAL SERVICE

Lieut. Col. Pope B. Holliday, chief of dental service.
Major George R. King, assistant chief of dental service.
Capt. John C. Breuker Jr., dental officer.
1st Lieut. Robert E. Connell, dental officer.
1st Lieut. Michael L. Di Napoli, dental officer.
1st Lieut. Julius Eingorn, dental officer.

VISIT BY GENERAL MORGAN

Brig. Gen. Hugh Jackson Morgan, Medical Department, who was professor of medicine at Vanderbilt University, Nashville, Tenn., before called to duty as chief consultant in medicine in the Surgeon General's Office, Washington, D. C., on March 10, completed a visit at Carlisle Barracks, Pennsylvania, to study the work of the Medical Field Service School and the Medical Department Equipment Laboratory. General Morgan addressed the three basic officers classes on "The Mission of a Medical Officer." He was accompanied by Lieut. Col. B. Noland Carter, Medical Corps, assistant to the consultant in surgery in the Surgeon General's Office. In the first world war General Morgan, a senior at Johns Hopkins University, enlisted for service with Base Hospital No. 18 and was sent overseas in the American Expeditionary Forces. In May 1918 he was commissioned a first lieutenant in the Medical Corps at Longres, France. Colonel Carter was assistant professor of surgery at the University of Cincinnati before being called into military service about a year ago.

NUTRITION PROGRAM AT WRIGHT FIELD

A display of nutrition exhibits prepared by Dr. Bruno Gebhard and lent by the Cleveland Health Museum is the first step in a campaign designed to increase the efficiency of workers and reduce sickness "absenteeism" at Wright Field, Ohio. The opening phase of the campaign came with the announcement of food rationing, and it has given field workers information on selecting nutritious food within the rationing limits.

Illustrated in the exhibits are types of protective foods, caloric values of protective foods and the caloric requirements for eighteen different activities in the home, at work and at play; also shown are values of food containing iron, calcium, protein and vitamins; other exhibits expose common food fallacies and show how to get double food value for less money. The nutrition exhibit is based on five rules for a good lunch:

1. Your lunch should give you one third of your total daily food.
2. It should include milk in some form.
3. It should include whole grain.
4. It should include some kind of protein, as meat, eggs, cheese or beans.

Specially prepared pamphlets on nutritional problems, including planned diets, have been made available to field workers under the new program. Heading the health and nutrition program at Wright Field is Major Zolton T. Wirtschafter, chief of the civilian Medicine and Industrial Hygiene Section and former instructor at the Cleveland City Hospital, Western Reserve University Medical School.

CLASS OF MEDICAL INSPECTORS

Forty-six medical officers, comprising the fourth class of medical inspectors, graduated March 13 from a special training course at the Medical Field Service School at Carlisle Barracks, Pennsylvania. Following the exercises, the men left for their new posts. The duties of medical inspectors are to supervise sanitation and other medical preventive measures in army camps. Twenty-two of the forty-six officers had graduated previously from the basic course for officers at the Medical Field Service School. The class included eight majors and thirty-seven captains, all of the Medical Corps, and one captain of the Sanitary Corps. The officers represented twenty-six states. Another class of medical inspectors numbering about fifty officers started on March 22.

ARMY LEASES PART OF MICHIGAN'S LABORATORY FACILITIES

Manufacture by the Army Medical Department of biologic products to be used by the Army, Navy and Coast Guard, using facilities of the Michigan Department of Health Laboratories in Lansing, is to begin soon. Leasing two floors of the new Groesbeck serum and vaccine laboratory building now nearing completion, the Army will use its own equipment. The Lansing laboratories of the state department will continue the manufacture of biologic products for state distribution and its other routine services.

NAVY

NEW NAVAL HOSPITAL FACILITIES

The Bureau of Medicine and Surgery of the U. S. Navy, Washington, D. C., announced on March 11 that three new hospital ships had been authorized and on March 5 that a new 1,000 bed naval hospital would be constructed at Pleasanton (Livermore), Calif. The Bureau of Medicine and Surgery at that time expected the early authorization of plans to expand the bed capacity of two other East coast and six West coast naval hospitals, including hospitals at Philadelphia, San Diego, Long Beach, Seattle, Treasure Island, Corona and Santa Margarita.

A new naval hospital with 1,500 beds was formally opened on February 15 in Queens, New York. The hospital had already admitted several hundred patients. The thirty-five wards are of one story wooden barracks type. The commanding officer is Capt. L. L. Pratt, U. S. N., and the executive officer is Capt. B. H. Adams. The superintendent of nurses is Lieut. Comdr. Anna Keating, U. S. N., and the seventy some medical officers on the staff are mostly prominent men in the various specialties. In all there are 71 nurses, 317 members of the navy hospital corps and 235 civilian employees. The hospital is built on one of the fine golf courses on Long Island and is complete in all respects for handling any class of patients. The community in this area and the national organizations have made many donations to the Red Cross unit of the hospital and to the Secretary of the Navy for various forms of equipment.

The U. S. Navy has opened a new hospital at Key West, Fla., and the Marine Hospital formerly in operation at Key West has been closed. Rear Admiral Luther Sheldon Jr. of the Navy Medical Corps, who recently inspected the naval medical facilities in the seventh naval district, reported that he was favorably impressed by the new hospital in Key West.

The Colorado Hotel at Glenwood Springs, Colo., is being prepared as a U. S. Navy hospital with a 500 bed capacity.

It was announced by representative Lex Green of Florida, February 25, that St. Mary's Hospital in West Palm Beach, which was built in 1938, will be taken over by the Navy.

NAVAL DENTAL CORPS REAR ADMIRAL

Recent legislation authorized the temporary appointment of a rear admiral in the dental corps of the U. S. Navy. A selection board met early in March at the Navy Department and selected for nomination as rear admiral Capt. Alexander Gordon Lyle, D. C., U. S. N. Dr. Lyle was born at Gloucester, Mass., in 1889, graduated from Baltimore College of Dentistry in 1912 and was commissioned lieutenant (jg) in the Dental Corps of the Navy in 1915. During the first world war Captain Lyle served with the marines in the second division in France and was awarded the Medal of Honor and two Silver Star medals for extraordinary heroism under fire. He served on various ships later and again with the marines in Shanghai, China, and for four years ended in August 1936 was head of the dental department of the U. S. Naval Hospital, Newport, R. I. The following year he completed the course in the Army Industrial College and recently has been head of the dental department of the Naval Air Station, Quenset Point, R. I.

WAVES FOR THE HOSPITAL CORPS

A Hospital Corps School for Waves to be established at the Naval Medical Center, Bethesda, Md., has been authorized and construction is expected to start soon. The school will accommodate training classes of 500 students. On March 8 there were 209 Hospital Corps Waves, of whom 97 were on active duty at that time and 122 were undergoing indoctrination at Bethesda and San Diego. The Bureau of Medicine and Surgery expected another 150 on March 22, which would be assigned to indoctrination classes at the naval hospitals at Great Lakes, Ill., New York and Chelsea, Mass. Another group of 150 waves was expected from the Wave School at Cedar Falls, Iowa, on April 5.

NAVAL MEDICAL NEWS LETTER

Bumed News Letter, edited by Capt. W. W. Hall, M. C., U. S. Navy, is issued by the Bureau of Medicine. The letter contains information of importance to all medical officers, especially those isolated by war from the usual sources of medical information. Abstracts of important articles in current medical and scientific periodicals are included. The present microfilm letter, reproduced from material supplied by the Committee on Medical Information of the National Research Council, Division of Medical Sciences, is incorporated with this publication. It is distributed by regular and by V mail to naval medical officers ashore and afloat.

NAVY PERSONALS

Dr. Lewis H. Wright, head of the department of anesthetics of E. R. Squibb & Sons, New York, entered the U. S. Naval Reserve with the rank of lieutenant commander on March 1. Dr. Wright joined the anesthetic department of E. R. Squibb & Sons in 1930 and for several years has been the head of that department.

Air Commodore C. P. Symonds of the R. A. F., consultant in neuropsychiatry, visited on March 18 the Bureau of Medicine and Surgery in Washington. Commodore Symonds was in the United States also for the purpose of giving the Dunham Lectures at Harvard University.

Lieut. Comdr. Clement C. Clay of the Navy Medical Corps Reserve has been assigned to the Personnel Division at the Bureau of Medicine and Surgery.

Lieut. Gerald J. Sullivan, M. C., U. S. Naval Reserve, has been assigned to duty at the Naval Dispensary in Washington.

Lieut. Comdr. Charles Wheatley, M. C., U. S. Navy, retired, has been assigned for duty to the correspondence course section at the Bureau of Medicine and Surgery.

Capt. Robert W. Wimberly, M. C., U. S. Navy, has reported for duty to the Naval Dispensary, Washington, D. C.

Comdr. Omar J. Brown, M. C., U. S. Navy, has been assigned as head of the new section of tropical medicine of the Division of Preventive Medicine of the Bureau of Medicine and Surgery, Washington, D. C., and Lieut. John F. Shronts, U. S. Naval Reserve, has been assigned to the section of Venereal Disease Control, replacing Lieut. George W. Mast, M. C., U. S. Navy, who has been assigned in charge of the section of audiovisual education.

Lieut. Comdr. W. H. Schwartz, M. C., U. S. Navy, has been assigned to the Venereal Disease Section in the Bureau of Medicine and Surgery, and Comdr. Ladislaus Adamkiewicz, M. C., U. S. Navy, to the research division.

MEDICAL FIELD SETS DONATED TO COAST GUARD

The Illinois Opera Guild Ferry Command and the Drake Hotel Red Cross Unit have presented emergency medical field sets to the U. S. Coast Guard at Chicago. In forwarding these sets from the Medical and Surgical Relief Committee of America in New York, Mrs. Huttleston Rogers, executive chairman, writes that the War Shipping Administration has made a request for twenty-four emergency medical field sets to be sent to Casablanca, Dakar, Cape Town, Murmansk, Trinidad and other distant ports. The Anglo-American Commission also has requested thirty-six of these units for use in the Caribbean area. The committee requests that physicians and surgeons, particularly, and any other persons who may have scalpels, splinter forceps, probes, grooved directors, scissors and other instruments of this nature send them promptly to the committee's headquarters at 420 Lexington Avenue, New York City. These instruments need not be new, as facilities are available for their repair.

CIVILIAN DEFENSE

BRITISH METHOD OF BLANKETING A CASUALTY

The British (Wanstead) method of blanketing casualties mentioned in Circular, Medical Series No. 20, U. S. Office of Civilian Defense, is described herewith. Using two blankets as described, there are four thicknesses beneath the patient and two above. The feet are tucked in and kept warm by the use of this technic, and the head is protected against cold. When the blanket fold is completed, it securely fixes the extremities and trunk so that it can be used as a blanket carry, if necessary.

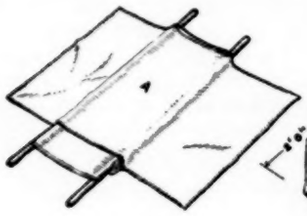


FIGURE 1

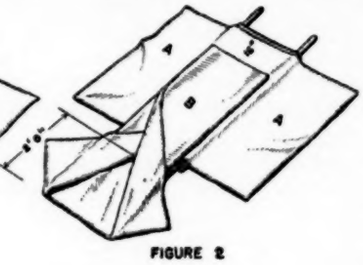


FIGURE 2

PREPARING THE STRETCHER

1. Place blanket *A* lengthwise across the stretcher with one side close to the head end of the stretcher, and one end of the blanket having a slightly longer overlap of the stretcher than the other end (fig. 1).

2. Fold blanket *B* in thirds lengthwise and place over *A*, the upper edge of this folded blanket being about 15 inches below the upper edge of blanket *A* (fig. 2). For very tall persons it is necessary to lay blanket *B* farther down on the stretcher to permit its lower end to extend a sufficient length below the patient's feet so that it may be folded up and around them in the manner to be described.

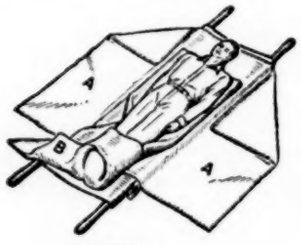


FIGURE 3

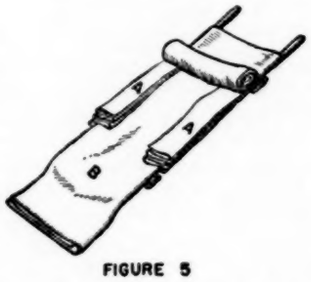


FIGURE 5

3. Open the folds of blanket *B* for about 2 feet at the foot end (fig. 2).

WRAPPING A PATIENT

1. Bring the foot of blanket *B* up over the feet, with a small fold between the feet.

2. Tuck the two open folds of blanket *B* closely over and around the feet and ankles (fig. 3).

3. Turn in upper corners of ends of blanket *A* (fig. 3), wrap shorter end of blanket *A* over patient and then the longer end and tuck well in at side (fig. 4).

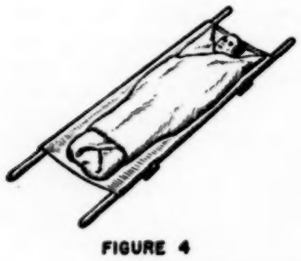


FIGURE 4

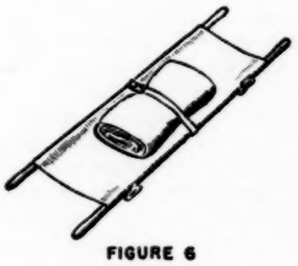


FIGURE 6

BLANKET ASSEMBLY FOR TRANSIT

1. Proceed as under 1 and 2 for preparing a stretcher.

2. Fold in the two ends of blanket *A* in accordion pleats (fig. 5); fold in the foot end of blanket *B;* then roll the blanket and make secure (fig. 6). A hot water bottle may be placed in the center of the blanket pack to keep it warm.

TRANSPORTATION FOR CASUALTIES

Transportation for casualties from scenes of disaster to hospitals and for injured persons or other patients removed from casualty receiving hospitals to emergency base hospitals is included in plans for emergency transport service during war disasters, described in recent operations letters issued by the Office of Civilian Defense.

Plans for local transportation are centered in the transport officer of the U. S. Citizens Defense Corps. It is the duty of the transport officer to maintain inventories of local equipment that can be used by the various emergency services of the Citizens Defense Corps, and he is responsible for organization, training and supervision of volunteer drivers' units. Such equipment may include passenger cars, station wagons, motorcycles, ambulances and other private vehicles.

Through joint action of the Office of Defense Transportation and the Office of Civilian Defense, local commercial motor vehicles, including taxicabs and trucks of small operators, which are now under the jurisdiction of the Office of Defense Transportation, have been released to the transport officer for local service in case of war emergency. He may make use of such vehicles immediately, without application to the ODT.

For transport facilities needed outside the local area, such as might be required for evacuation of civilians or for transfer of injured persons to emergency base hospitals in other areas, the OCD and the ODT are organizing motor transport units in the larger common, contract and private motor carriers of the critical areas of the country. These units will be trained in convoy service. ODT is developing an organization in the critical areas under which its district managers will make contact with the local transport officers to make certain that each community is organized to function under the plan.

Operations Letter No. 114, issued March 3, urges cooperative planning between the Citizens Defense Corps and the American Red Cross, the Women's Defense and Ambulance Corps and local or state automobile associations or clubs, in order that several agencies may not seek to mobilize the same equipment independently but may do so in cooperation.

IDENTIFICATION OF VEHICLES IN BLACKOUT

A uniform system of identification of emergency vehicles operating during real or practice air raid alarms was announced by the Office of Civilian Defense in Operations Letter No. 111. The primary identifying device is a white pennant measuring 18 inches along each side with a 6 inch basic Civilian Defense insigne; that is, the letters CD in red inside a white triangle superimposed on a red circle. The pennant is to be attached to the left front portion of the vehicle. To identify emergency vehicles at night, the operations letter prescribes a headlight mask over the right headlamp for use where blackout regulations permit the use of headlights; in coastal dimout areas it should be used in conjunction with dimout equipment. The design of the mask embodies the CD insigne 2½ to 3 inches in diameter in green.

Vehicles entitled to use the emergency identification include (*a*) vehicle of the armed forces of the United States or of the Allies or other vehicles acting under orders, (*b*) vehicles of fire departments and governmental police agencies, (*c*) ambulances and rescue cars and other vehicles converted to such use in emergency services, (*d*) public utility repair vehicles operating in emergency service and (*e*) vehicles in emergency service as defined by state civilian defense authorities.

The operations letter recommends that all states adopt the definition of emergency motor vehicles and the methods of identification prescribed. Although many states have already adopted different methods of identifying emergency motor vehicles, it was urged that all states adopt the new devices. A uniform system is important in order that emergency motor vehicles which may be crossing state lines may not face unnecessary interference.

MISCELLANEOUS

AN APPEAL FOR EMERGENCY MEDICAL SUPPLIES

The medical supplies on the French warships now in our ports for repairs are seriously depleted and, at the request of the chief medical officer of the battleship *Richelieu*, the Medical and Surgical Relief Committee of America, with headquarters at 420 Lexington Avenue, New York City, has supplied the ship with a complete operating set, including rubber gloves, sutures, needles, antiseptics, thermometers and vitamins.

The chapter of the American Women's Voluntary Services in Winter Park, Fla., has sent to the Medical and Surgical Relief Committee twelve submarine chaser medical kits, three emergency medical field sets and thousands of dressings.

At the request of the British War Relief, the Medical and Surgical Relief Committee of America has sent twelve complete dental units, one hundred extraction forceps and one hundred hypodermic syringes and needles to North Africa.

The Washoe County Medical Society has raised funds to purchase a complete operating set and emergency medical field set for use on board the cruiser *Reno*. The presentation was made at the headquarters of the Medical and Surgical Relief Committee of America, New York City, to a representative of Rear Admiral Melhorn of the Navy Medical Supply Depot in New York.

Many women's clubs throughout the country are conducting special campaigns by placing collection tins and posters in department stores in which the public may donate old scissors, knives, safety pins, bandages, tweezers and fishing tackle for forwarding to the Medical and Surgical Relief Committee of America at 420 Lexington Avenue, New York City, where they will be repaired if necessary and used to equip emergency kits for use on submarine chaser and coast guard patrol boats.

MORE NURSES NEEDED

At a meeting of the directors of the National Nursing Council for War Service in New York, March 19, it was reported that schools of nursing throughout the country admitted 5,000 more students during the current year than they did the year before. However, the total of 49,169 is nearly 6,000 less than the quota which the nursing profession and the government estimated necessary to meet war needs.

"Since 6,000 young women who were needed as nurses are doing something else instead or taking no part in the war effort," said Katherine Faville, chairman of the Council's Committee on Recruitment of Student Nurses, "some new element must be added if we are to secure the greatly increased number of new students, 65,000, who should begin nursing educations during the school year that opens June 1. The modest government stipends for student nurses that it suggests should enable more of those qualified to enter nursing and should help meet the competition of high salaried war industry or the various military auxiliary services which offer women a soldier's pay even during training."

The school admissions figures were reported by the Department of Studies of the National League of Nursing Education on the basis of questionnaires sent to the 1,300 state accredited schools of nursing in the country. The admissions for the period June 1, 1942 to June 1, 1943 total 49,169, or 89 per cent of the quota sought. Eight states reached or passed the quotas assigned to them. They are Arkansas, Idaho, Iowa, Minnesota, New Mexico, North Carolina, Oklahoma and West Virginia. Other states which reached 90 per cent or more of their quotas are California, Colorado, Delaware, District of Columbia, Illinois, Indiana, Maine, Massachusetts, Mississippi, Montana, Ohio, Pennsylvania, Rhode Island, Utah and Virginia. The New York State percentage was 86. The Committee on Recruitment of Student Nurses, now launching a heightened spring campaign, will study the areas where success was achieved in comparison with states where fewer girls entered nursing, to seek light on reasons, and to devise better methods.

HEALTH UNDER HITLER

It is reported from Presov, according to *Grenzbote*, Bratislava, of Nov. 24, 1942, that all persons between 2 and 80 were compulsorily inoculated against typhus. Simultaneously the inoculation of all dogs against rabies was decreed.

Donauzeitung, Belgrade, of Nov. 12, 1942 reports that the Rumanian cabinet has resolved to set up a commission to purchase medical supplies, bandages and medical instruments. This purchasing commission has been instructed to purchase the necessary materials for the social central insurance office from Germany and Italy.

DNB of January 7 states that the systematic care for the health of young persons has now been enriched by a work unique in various respects and of fundamental significance for the future. It is the "Principles Laid Down by the Reich Health Leader and Reich Youth Leader on Health Services for Youth," which the reich minister of the interior has made obligatory. For the first time a large scale scheme which comprises an entire nation and makes use of all means at the disposal of modern science has been devised providing for periodic free medical examinations for all boys and girls from their sixth to their eighteenth year as a joint task of the party and the state. During the war this health scheme will comprise only certain age groups, while it is to be put into practice fully after the war. In his introduction, Conti states that care for the health of youths is the core of the entire health service. It constitutes, as Reich Youth Leader Axmann points out in his preface, one of the foundations of the work of the Hitler Youth, and its promotion should be the main task of every doctor and youth leader. A sufficient number of doctors for juveniles will have to carry out the medical service according to the "Principles." The task of the official (staatlich) doctor for juveniles —a profession now coming into existence—is one of the highest responsibility toward the community. To start with, a series of five examinations is envisaged for peacetime. The juveniles are to be examined at the ages of about 6, 10, 14, 15 and 18. To this must be added five to six "medical roll calls" for children up to the age of 14 and, furthermore, yearly "dental roll calls." The examinations are based on the youth health record sheet, which is uniform throughout the reich; the latter is covered by the doctor's obligation for secrecy, and every child from his sixth to his eighteenth year will have one.

The wartime reich physician of the Hitler Youth, Ministerialrat Dr. Liebenow, who compiled the "Principles" in collaboration with competent authorities, calls this series of examinations the core of the Youth Health Service. These examinations, which make use of x-ray photography too, deal with the juvenile's general constitution, environment, internal organs, sight and hearing, muscles, skeleton, wrong carriage, complexion —in short, with everything which is significant for a general medical supervision. The examinations pursue the following aims: exact medical reports which take into consideration hereditary factors; assessing physical capacities; making available measures necessary to improve the state of health; entries into fitness certificates in which the points that call for consideration are stated as far as necessary, and the supply of material for the health statistics concerning the juvenile population. In the case of the 10 year old child it will be possible to include at the same time a statement on the child's fitness to join the "Jungvolk," or the "Jungmadelbund," or for the hauptschule, while with regard to the 14 year old child his fitness for work will be stated. In the case of the 15 year old child attention will be paid to the influence of the first year of employment on his working capacity and development. It is left open to the parents to give written information regarding the wishes or ailments of the child. The "medical roll calls" are intended to fill the gaps between the series of examinations as far as is possible. The doctor for juveniles is expected to discern health defects at an early stage and give helpful advice for the child's development, while any actual medical treatment which may become necessary is to be left to the doctor chosen by the family.

ORGANIZATION SECTION

OFFICIAL NOTES

ABSTRACT OF MINUTES OF MEETINGS OF BOARD OF TRUSTEES HELD FEB. 18-19, 1943

Careful consideration was given to the business of the Association at the annual meeting of the Board of Trustees, which was held in the headquarters office on February 18-19, preceded by a full day meeting of the Executive Committee.

FURTHER TRAINING OF PHYSICIANS BOTH IN AND OUT OF THE ARMED FORCES

The Board voted to sponsor plans for the further training of physicians both in and out of the armed forces, in cooperation with the American College of Physicians and the American College of Surgeons. It elected Dr. Edward L. Bortz of Philadelphia to act as its representative and made an appropriation to aid in putting the plan into effect.

NATIONAL CONFERENCE ON PLANNING FOR WAR AND POSTWAR MEDICAL SERVICES

The Board also voted to cooperate with other organizations in the medical and allied fields in sponsoring a conference on planning for war and postwar medical services, to be held in New York on March 15.

POSTWAR PLANS FOR MEDICAL CARE

Drs. Roger I. Lee (Chairman), James E. Paullin, Fred W. Rankin and H. H. Shoulders were appointed a committee on postwar plans for medical care with authority to enlarge the committee to eight or more persons. This committee will cooperate with similar committees which will be appointed by the American College of Physicians and the American College of Surgeons.

DINNER FOR HOUSE OF DELEGATES

The Executive Committee was authorized to arrange for a dinner for the House of Delegates on Monday evening, June 7, and for a meeting immediately thereafter to which will be invited as guest speakers persons who can inform the House on questions of current interest; and if, because of war restrictions, it is impossible to arrange for a dinner, to plan simply for the evening meeting with guest speakers.

RECORDING OF BROADCASTS FOR THE USE OF COUNTY SOCIETIES

Authorization was given by the Board for the recording of some of the interview programs over WLS under the title "Before the Doctor Comes," in which Dr. W. W. Bauer is cooperating, and for procuring copies of each recording with a view to furnishing these to county medical societies or local stations which may at the present time have difficulty in securing persons to broadcast.

APPROPRIATIONS

Appropriations were made for the conduct of the work of the various councils, bureaus and departments in the headquarters office, for regularly held conferences, for the committees on Scientific and Therapeutic Research and for some special research projects.

COMMITTEE ON CONSERVATION OF VISION

The Committee on Conservation of Vision and Prevention of Blindness that was appointed by the Board of Trustees in 1940 in accordance with a resolution from the Section on Ophthalmology adopted by the House of Delegates, which has failed to function, was discontinued by the Board and a new Committee on Conservation of Vision was appointed consisting of Dr. Lawrence T. Post, St. Louis; Dr. Conrad Berens, New York; Dr. J. V. Cassady, South Bend, Ind.; Dr. E. C. Ellett, Memphis, Tenn.; Dr. Harry S. Gradle, Chicago, and Dr. R. S. Irvine, San Francisco.

INVESTMENTS

Consideration was given to the matter of investing some of the funds of the Association, and a selection of eight bonds was made to add to the Association's portfolio.

APPOINTMENTS

The following appointments were made to fill vacancies on various councils, committees and editorial boards (the appointee succeeded himself unless it is otherwise stated):

American Journal of Diseases of Children, Dr. Oscar M. Schloss; Dr. A. A. Weech of Cincinnati to succeed Dr. A. Graeme Mitchell (deceased), and Dr. James L. Wilson of Detroit to succeed Dr. Horton R. Casparis (deceased). *Archives of Dermatology and Syphilology,* Dr. C. Guy Lane. *Archives of Ophthalmology,* Dr. David G. Cogan. *Archives of Pathology,* Dr. James Ewing. *Archives of Surgery,* Dr. Arthur W. Allen, and Dr. Albert J. Scholl of Los Angeles to succeed Dr. Wallace I. Terry (resigned). *Archives of Internal Medicine,* Dr. N. C. Gilbert. *Archives of Otolaryngology,* Dr. Ernest M. Seydell of Wichita, Kan., to succeed Dr. W. P. Wherry (deceased). *Archives of Neurology and Psychiatry,* Dr. Wilder Penfield, and Dr. Charles D. Aring of Cincinnati to succeed Dr. S. W. Ranson (deceased). Council on Physical Therapy, Dr. John S. Coulter, Dr. W. W. Coblentz and Dr. W. E. Garrey. Council on Foods and Nutrition, Dr. George R. Cowgill and Dr. Lydia J. Roberts. Council on Pharmacy and Chemistry, Dr. H. N. Cole, Dr. C. S. Keefer and Dr. Stuart Mudd. Council on Industrial Health, Dr. Leverett D. Bristol, Dr. Stanley J. Seeger and Mr. Philip Drinker. Committee on Scientific Research, Dr. John J. Morton. Committee to Study Air Conditioning, Dr. Alvan L. Barach of New York as an additional member. Joint Committee on Health Problems in Education of National Education Association and American Medical Association, Dr. A. J. Chesley. American Documentation Institute, Dr. Ludvig Hektoen, Chicago. Foundation for the Study of Cycles, Dr. Kenneth Maxcy. Special Committee on Hospital Libraries, Dr. William G. Hibbs, Chicago.

DISCONTINUATION OF TRANSACTIONS OF SECTION ON LARYNGOLOGY, OTOLOGY AND RHINOLOGY

Authorization was given for the discontinuation of the Transactions of the Section on Laryngology, Otology and Rhinology unless the number of orders is increased sufficiently to indicate that specialists in this field are interested in having the Transactions in book form.

UNITED STATES OF AMERICA V. AMERICAN MEDICAL ASSOCIATION

The Board unanimously adopted the following statement regarding the decision of the Supreme Court of the United States in the case of the *United States of America* v. *the American Medical Association and the Medical Society of the District of Columbia:*

The decision of the Supreme Court in regard to the case involving the Medical Society of the District of Columbia and the American Medical Association was announced January 18 and was published in THE JOURNAL on January 23. On the advice of Counsel a check for $2,500 has been sent to pay the fine assessed by the District Court against the American Medical Association. Following further advice of Counsel, analysis or interpretation of this decision has not been made.

The policies of the American Medical Association in the standardization of medical education, hospitals or other aspects of medical care are established by the House of Delegates. In the conduct of its defense in this case the Board acted on the authority of the House of Delegates, in each instance given unanimously.

Many other subjects were discussed some of which will receive further consideration in the future.

MEETING OF THE COUNCIL ON INDUSTRIAL HEALTH

The eleventh meeting of the Council on Industrial Health was held on January 10 at the Palmer House in Chicago. Council members in attendance were Stanley J. Seeger, chairman; Harvey Bartle, Leverett D. Bristol, Warren F. Draper, Philip Drinker, Leroy U. Gardner, Raymond Hussey, Anthony J. Lanza, Robert T. Legge, Clarence D. Selby, William D. Stroud and Carl M. Peterson, secretary.

REPORT OF THE COMMITTEE ON RULES

The Committee on Rules presented a report, rearranging the tenure of service of members of the Council on Industrial Health at four years, so staggered that three appointments expire each year.

REPORT OF THE COMMITTEE ON NOMENCLATURE

After extended discussion the Council resolved (1) to defer publication of the dictionary on industrial health until Dr. Henry Kessler can resume active direction, (2) that the Council discharge its current obligations for services rendered in this direction, (3) that the material remain in the chairman's hands for such additions and revisions as may profitably be added from time to time and (4) that a small additional appropriation be requested as recompense for additional editorial and clerical services.

REPORT OF COMMITTEE ON PROFESSIONAL RELATIONSHIPS

Since early February, forty-two state medical societies have been visited, eighteen of them two or more times. Seven state medical societies appointed committees on industrial health during the year, making a total of forty-five. Loss of committee members to military service and for other reasons required reorganization of the established committees in eight states.

Field procedure in the various states depended on the amount of previous activity and the needs of the area. In almost every state the chairman and members of the committee on industrial health, secretary and other officers of the state medical society, and the bureau of industrial hygiene were visited. Where indicated and possible, the deans of medical schools, state health commissioners and industrial organizations were contacted. Emphasis was placed on better health in relation to war production, the need for better medical organization and leadership, education of the medical profession, industry and other interested agencies, and active cooperation with state procurement and assignment agencies in solving medical problems in industry.

Similar activities are planned for the coming year assisted, as soon as possible, by additional personnel already authorized by the Board of Trustees. It is planned to stimulate reorganization of those state committees which have not been active and to encourage broader and more comprehensive programs in those which have shown progress.

The advisory committees representing the sections in the Scientific Assembly of the American Medical Association are of great assistance to the Council in its educational and organizational activities. This phase of the program will be pressed during the months ahead.

Considerable discussion occurred about the status of the Council in relation to the War Participation Committee of the A. M. A. respecting (1) local organization for industrial health service in a small plant and (2) a program of training and procurement of physicians for industry.

Principal concern referred to recent arrangements under which the U. S. Public Health Service and the Procurement and Assignment Service will jointly undertake studies of war industry and extracantonment areas from which shortages of medical and allied professional personnel are reported. As reported, these studies shall be made jointly by the Procurement and Assignment Service and representatives of the U. S. Public Health Service. The state medical society and the state health department will each be invited also to designate a representative to participate in such studies.

In the discussion of this important statement of policy, the Council received instruction on two main points: (1) whether this language superseded past resolutions of the Procurement and Assignment Service which called on the Council on Industrial Health and the state medical society committees on industrial health to undertake certain functions in respect to procurement training and assignment of physicians for industry, and (2) whether this statement coincided with sentiment developed through field activity of the Council that the resources of county and state medical societies had not been fully explored as a means for bringing willing physicians and industrial opportunities together.

Reassurance was received that such facilities as the Council and its cooperating state agencies could bring to bear on this troublesome problem would be welcome. It was further suggested that the Central Board of Procurement and Assignment should be asked to reinform its regional and state chairmen to this effect.

REPORT OF COMMITTEE ON EDUCATION AND PUBLICATIONS

Evidence was presented indicating that additional progress had been made in the development of courses of instruction in medical schools. A syllabus for a course in industrial health recently submitted to all approved medical colleges in the United States and Canada was ordered to be revised according to new advances made in the field.

The report also reviewed progress in postgraduate industrial medical teaching, ranging from refresher courses to intensive teaching. Attention was called to the fact that there are at the present time no training appointments in the industrial field offering acceptable internship or residency experience. It was thought desirable to approach the Council on Medical Education and Hospitals for advice and encouragement along these lines.

The desirability of preparation of local health officers for industrial hygiene was reaffirmed as a means toward better acquaintance with industrial health problems by the profession at large. Particular mention was made of the difficulties of establishing a certification program in the industrial health field and the present status of that program.

The Council noted with interest the progress made toward the development of a joint program with the Council on Pharmacy and Chemistry with a view to preparing and publishing an industrial medical formulary. Steps required to appoint a suitable committee representing the Council on Industrial Health and the presentation of a proper request to the Council on Pharmacy and Chemistry in order that a similar subcommittee be set up in that body were approved.

The secretary was also instructed to obtain advice and active cooperation from the Bureau of Health Education of the A. M. A. in respect to a program of health education for labor organizations.

REPORT OF COMMITTEE ON PHYSICAL EXAMINATIONS

In consideration of the importance of industrial physical examinations, the committee was asked to continue its consideration of the subject with a view toward publication of a report at the earliest possible time.

REPORT OF COMMITTEE ON OCCUPATIONAL DISEASE REPORTING

The Council registered its understanding that occupational disease reporting included absenteeism studies and expressed the hope that recommendations may be developed to improve medicine's contribution in this field.

REPORT OF COMMITTEE ON WORKMEN'S COMPENSATION

A program for coordination of effort between the Council on Industrial Health, the Bureau of Legal Medicine and Legislation and the Council on Physical Therapy in the related fields of workmen's compensation and rehabilitation was regarded as a definite step forward.

The preparation of reviews concerning best prevailing medical opinion on medical subjects having some legal connotation was again proposed. It is the intention of the committee to proceed along these lines at the earliest opportunity. In this connection again the necessity for close cooperation with the Bureau of Legal Medicine and Legislation was emphasized.

The committee also recommended, as a possible development for the future, a special conference to discuss the whole problem of workmen's compensation with regard to improved medical relationships and many other details of administration. Augmentation of the present personnel of the Committee on Workmen's Compensation to include experts in the fields of medicine, management, insurance, labor and others was looked on as urgently necessary.

It was pointed out that the National Tuberculosis Association is attempting to collaborate with the Council through the appointment of editorial writers to introduce the subject of industrial medicine in monthly publications. In addition, the Trudeau Society has appointed a Committee on Industrial Tuberculosis.

REPORT OF COMMITTEE ON RESEARCH

The chairman reported several conferences with the chairman of the Committee on Occupational Pathology regarding the development of a registry of lung tissue from persons subjected to various industrial exposures.

The Committee on Research was instructed to interest itself in the possibility of clinical investigation through the cooperating committees in the sections of the A. M. A. and the availability of funds within the Association itself for the carrying on of such research.

REPORT OF COMMITTEE ON AVIATION MEDICINE

The Council discharged its Committee on Aviation Medicine.

INDUSTRIAL NURSING

The Council ordered the preparation of an Outline of Procedure for Nurses in Industry. It was recommended that in the preparation of this material special care be taken not to duplicate activity taking place in other organizations. In this connection, consideration was given data submitted by the Committee to Study the Duties of Nurses in Industry of the Nursing Section of the American Public Health Association.

NUTRITION IN INDUSTRY

The first meeting of the Joint Committee on Nutrition in Industry, made up of representatives from the Council on Industrial Health and the Council on Foods and Nutrition was described, together with plans for a symposium on nutrition in industry to be sponsored by this committee at the fifth Annual Congress on Industrial Health.

INDUSTRIAL MEDICAL SERVICE PLANS

As soon as conditions warrant, information will be collected from likely sources on industrial medical service plans.

LABOR ORGANIZATIONS AND INDUSTRIAL HEALTH

The general impression was that there should be closer contact with labor organizations and that some effort should be made to enlist their cooperation, both in the maintenance of industrial health services within the plant and in general programs of health education covering nonoccupational disability.

REHABILITATION COUNCIL

The attention of the Council was directed to the formation of a Rehabilitation Council representing thirty-eight national agencies interested in the vocational and reconstructive phases of rehabilitation. Because of the Council's interest in the subject, and because the Council on Physical Therapy is represented on the Rehabilitation Council, and since, furthermore, the question of rehabilitation will be of unusual importance during the present legislative year, it was decided to create a liaison committee with the Council on Physical Therapy as a means of maintaining close contact with activities in the rehabilitation field and for the purpose of formulating reports and specific recommendations.

THE U. S. MARITIME COMMISSION

The U. S. Maritime Commission wishes to enlist the help of the Council on Industrial Health to instruct physicians in the neighborhood of shipyards about special care required for workers who suffer from exposures which may not manifest themselves until after the men have left work.

THE U. S. CHAMBER OF COMMERCE

Plans for an advisory health council in the Chamber of Commerce of the United States were described, with particular reference to a subcommittee on industrial health and the possibilities for integrated educational programs for employers and physicians.

Dr. Stanley J. Seeger and Dr. Raymond Hussey were unanimously reelected as chairman and vice chairman respectively.

Names were submitted as nominations for expired terms in accordance with recently revised rules of the Council.

The next meeting of the Council was set tentatively for Sunday, June 6, in Chicago, just preceding the meetings of the House of Delegates.

DOCTORS AT WAR

Radio broadcasts of Doctors at War by the American Medical Association in cooperation with the National Broadcasting Company and the Medical Department of the United States Army and the United States Navy are on the air each Saturday at 5 p. m. Eastern War Time (4 p. m. Central War Time, 3 p. m. Mountain War Time, 2 p. m. Pacific War Time). An exception is the Chicago area, where the broadcasts are heard by transcription at 10:30 p. m. Saturdays over Station WMAQ.

The titles and guest speakers for the next four programs are as follows:

April 17. "Stratosphere Flight."
Speaker, Brig. Gen. David N. W. Grant, Air Surgeon, United States Army.

April 24. "Sharp Eyes."
Speaker, Lieut. Col. Harold C. Lueth, Liaison Officer, Surgeon General's Office, United States Army.

May 1. "Jungle Death."
Speaker, Brig. Gen. C. C. Hillman, Chief of the Professional Services, Office of the Surgeon General, United States Army.

May 8. "Drugs March to War."
Speaker, Dr. Austin E. Smith, Secretary, Council on Pharmacy and Chemistry.

BEFORE THE DOCTOR COMES

The American Medical Association program on Radio Station WLS (890 kilocycles) entitled "Before the Doctor Comes" will be on the air every Thursday morning at 9:45 up to and including May 27. Mrs. June Merrill will interview Dr. W. W. Bauer, Director of the Bureau of Health Education, Dr. Edwin P. Jordan, Assistant Editor of THE JOURNAL, or Dr. Austin E. Smith, Secretary of the Council on Pharmacy and Chemistry, on common home health problems. The titles for the next four programs are:

April 15. "The Listless or Irritable Child." (Jordan.)

April 22. "What to Do About Bad Bumps." (Bauer.)

April 29. "What to Do About Bleeding." (Bauer.)

May 6. "What to Do About Foreign Bodies in Nose, Ears, Throat or Eyes." (Smith.)

MEDICAL ECONOMIC ABSTRACTS

RETURN AND PAYMENT OF VICTORY TAX BY EMPLOYER

Physicians who have withheld the victory tax from wages paid employees must make a return and transmit that tax to the collector of internal revenue having jurisdiction on or before April 30, using form V-1, Return of Victory Tax Withheld. This form may be obtained from the collector's office and must be signed and sworn to by the employer. The duplicates of receipts given employees (form V-2) need not be forwarded to the collector at this time; they should be retained by the employer until the final return is made for the year, on or before Jan. 31, 1944. In view of the severe penalties that may attach in event an employer neglects to transmit the withheld victory tax on or before the required date, physicians should transmit promptly the tax withheld during the months of January, February and March of this year.

MEDICAL CARE FOR WIVES AND CHILDREN OF ENLISTED MEN

The President on March 18 approved a deficiency appropriation bill making available to the Children's Bureau $1,200,000 for grants to states to provide medical, nursing and hospital maternity and infant care for wives and infants of enlisted men in the armed forces of the fourth, fifth, sixth and seventh grades. This appropriation will permit the continuation until June 30 of a program initiated last year and financed to date by federal allotments totaling $390,177 set aside from the regular appropriation authorized for maternal and child health services under part 1, title V, of the Social Security Act. No more funds were available from that source; hence the appeal to Congress for this deficiency appropriation. Legislation is pending in Congress to authorize additional funds so that the program may extend beyond the present fiscal year.

Regulations have now been promulgated by the Department of Labor, dated March 26, for the allotment of the $1,200,000 to the several states.[1] These regulations provide that the sums paid to the states for emergency medical and infant care shall be used exclusively for medical, nursing and hospital maternity and infant care for wives and infants of enlisted men in the armed forces of the United States of the fourth, fifth, sixth or seventh grades, for whom similar care is not readily available from the medical or hospital facilities of the Army or Navy or from facilities provided by or through official state or local health agencies. The Secretary of Labor will allot to each state submitting a plan approved by the chief of the Children's Bureau a sum based on the estimated number of applications for care during the period covered by the plan and the estimated cost of providing such care. A state plan must, among other things, provide that the cost of administration in the state will be met from funds other than the sums allotted for emergency maternity and infant care, that emergency maternity and infant care will be authorized under the plan as requested by or in behalf of any wife or infant of an enlisted man in the indicated grades, irrespective of legal residence, when similar care is not otherwise readily available and must provide for cooperation with medical, nursing and welfare groups and organizations.

The chief of the Children's Bureau, Katharine F. Lenroot, appeared before a subcommittee of the House Committee on Appropriations, February 11, in support of the request for this additional appropriation. She pointed out that plans at that time had been approved and programs were going forward in twenty-seven states and that similar programs would be developed in at least sixteen additional states if more funds become available. A table was supplied to the subcommittee indicating that for the period August 1942 to February 1943 a total of 2,840 obstetric cases had been authorized for medical and hospital care in twenty-one states. Experience obtained during the then five past months, Miss Lenroot said, showed that the demand for services was very great and that the sums available had not been sufficient to enable some states to accept all the cases for which application had been made. While the exact data on waiting lists were not available from all the states, it was known that one state had in December 1942 a waiting list of 300 and another of 400. Still another state was receiving applications at the rate of 12 a day and estimated an increase to 20 a day. At the request of the chairman of the subcommittee, Miss Lenroot inserted in the record the requirements exacted of a state board of health as a condition to cooperation on the part of the Children's Bureau in connection with this program. The following was submitted in compliance with that request:

> The Children's Bureau has informed the state health departments that the state plans for obstetric or pediatric medical and hospital care for women or children when the father is an enlisted man of the fourth, fifth, sixth or seventh grades in the Army of the United States, the United States Navy, the Marine Corps or the Coast Guard should provide efficient methods of administration of the plan by the state health agency, including acceptance of cases regardless of legal residence, the establishment of methods of authorization for medical or hospital care, methods of referral of cases to public health nursing and social services as needed, the establishment of fixed rates of reimbursement for services rendered under the plan, safeguards of the quality of medical and hospital care.
>
> Grants-in-aid will be made quarterly to the states on the basis of (1) current experience in each state with respect to the number of birth certificates issued showing the father to be in military service, (2) the cost of service per case within limits based on average cost of care for the area and (3) the number of authorizations per month.
>
> It is expected that the administration of these funds will be in accordance with the conditions laid down in the Social Security Act, title V, part 1, section 503 (a), items (2) through (6) inclusive, under which the existing services comparable to those to be provided under this proposed appropriation are now administered.

1. 8 Fed. Reg. 3859, March 30, 1943.

WOMAN'S AUXILIARY

WOMAN'S AUXILIARY TO THE AMERICAN MEDICAL ASSOCIATION

Twenty-First Annual Meeting, June 7-9, 1943
Drake Hotel, Chicago

A most cordial invitation is extended to all Auxiliary members and the wives of physicians attending the American Medical Association meeting to attend the sessions of the twenty-first Annual Meeting of the Woman's Auxiliary to the American Medical Association. Mrs. Rollo K. Packard is chairman of the Chicago Committee.

Headquarters will be in the Grand Ballroom of the Drake Hotel, where all meetings will be held. Please register early and obtain your badge and program. Tickets may be purchased at the registration desk.

All meetings will convene at the time scheduled. Please be prompt.

Registration, in the French Room Foyer:

Sunday, 2 to 4 p. m.
Monday, 8:30 a. m. to 4 p. m.
Tuesday, 8:30 a. m. to 4 p. m.

Preconvention Meetings

SUNDAY, JUNE 6

3 p. m. Nominating Committee meeting, Parlor H (east mezzanine), chairman Mrs. Robert E. Fitzgerald.

7 p. m. Finance Committee meeting, chairman Mrs. Harold F. Wahlquist.

PROGRAM

MONDAY, JUNE 7

9 a. m. Meeting of the Board of Directors, Parlors F-G (east mezzanine), Mrs. Frank N. Haggard presiding.

12:30 p. m. Luncheon in honor of the past presidents of the Woman's Auxiliary to the American Medical Association, Gold

Coast Room. Tickets $2.25 (subject to market conditions and food administration regulations). Guest speaker Dr. Frank P. Hammond, chairman of the Advisory Committee of the Woman's Auxiliary to the Illinois State Medical Society. Subject Doctors' Wives—Medicine's Closest Ally.

Convention Meetings

MONDAY, JUNE 7

2 p. m. Opening meeting of the House of Delegates of the Woman's Auxiliary to the American Medical Association, Grand Ballroom (lobby floor east), Mrs. Frank N. Haggard, President.

Invocation. Rev. Harrison Ray Anderson, Fourth Presbyterian Church, Chicago.
Address of Welcome. Hon. Edward J. Kelly, mayor of Chicago.
Tribute to Deceased Members.
Introduction of Mrs. Rollo K. Packard, chairman of the Chicago Committee.
Presentation of the President-Elect, Mrs. Eben J. Carey.
Minutes of the Twentieth Annual Meeting. Mrs. Carlton F. Potter, Secretary.
Roll Call. Mrs. Carlton F. Potter.
Convention Rules of Order. Mrs. Silas S. Smith.
Credentials and Registration. Mrs. Arthur I. Edison.
President's Message. Mrs. Frank N. Haggard.
Reports of Officers:
Recording Secretary, Mrs. Carlton F. Potter.
Corresponding Secretary, Mrs. Scott C. Applewhite.
Treasurer, Mrs. David W. Thomas.
Auditor, to be read by the recording secretary.
Reports of Directors:
Mrs. R. E. Mosiman.
Mrs. James P. Simonds.
Mrs. John Baron Farley.
Mrs. W. K. West.
Mrs. Frank L. Davis.
Mrs. David B. Allman.
Mrs. William J. Butler.

TUESDAY, JUNE 8

9 a. m. General session of the Woman's Auxiliary to the American Medical Association, Grand Ballroom, Mrs. Frank N. Haggard presiding.

Minutes. Mrs. Carlton F. Potter.
Announcements.
Credentials and Registration. Mrs. Arthur I. Edison.
Resolutions. Mrs. James P. Simonds.
Reports of Chairmen of Standing Committees:
Finance, Mrs. Harold F. Wahlquist.
Hygeia, Mrs. George R. Dillinger.
Legislation, Mrs. Luther H. Kice.
Organization, Mrs. T. Mitchell Burns.
Press and Publicity, Mrs. George H. Ewell.
Program, Mrs. William Hibbitts.
Public Relations, Mrs. Frank P. Dwyer.
Revisions, Mrs. Eustace A. Allen.
Report of Historian. Mrs. John J. Ryan.
Report of Bulletin Circulation and Central Office. Miss Margaret Wolfe.
Reports of state presidents.

12:30 p. m. Luncheon in honor of Mrs. Frank N. Haggard, President, Gold Coast Room. Tickets $2.25 (subject to market conditions and food administration regulations).

Guest Speakers: Brig. Gen. Fred Rankin, President, American Medical Association; Dr. James E. Paullin, President-Elect, American Medical Association; Dr. Morris Fishbein, Editor, THE JOURNAL and HYGEIA.

MEDICAL LEGISLATION

MEDICAL BILLS IN CONGRESS

Change in Status.—S. 400 has passed the Senate, a bill to reorganize the United States Public Health Service. The amendment declaring osteopaths eligible for appointment as reserve officers in the service was retained in the bill as passed by the Senate.

Bills Introduced.—S. 927, introduced by Senator Thomas, Oklahoma, provides that the amount of disability compensation or disability allowance payable to any veteran under the World War Veterans' Act, 1924, as amended and supplemented, shall not be reduced if such veteran (1) has attained or hereafter attains the age of 40, and (2) has received for a total period of five years or more disability compensation or a disability allowance for total permanent disability resulting from tuberculosis. H. R. 2308, introduced by Representative Lesinski, Michigan, provides vocational rehabilitation for members of the Regular Establishment after termination of hostilities in the present war. H. R. 2326, introduced by Representative Bolton, Ohio, provides that for the purpose of assuring a supply of nurses for the armed forces, governmental and civilian hospitals, health agencies, and war industries there will be authorized such annual appropriations as may be necessary. Such sums will be used in making payments to schools of nursing or other institutions which have submitted and had approved by the Surgeon General of the United States Public Health Service plans for nurses' training. A plan for training of nurses may be limited to student-nurse training or to postgraduate or refresher-nursing courses or may include both. The plans to be approved must provide, among other things, that the institution will pay student nurses a stipend at not less than the following monthly rates: $15 for the first nine months of study; $20 for the following fifteen to twenty-one months of combined study and practice, depending on the curriculum of the institution. A plan must provide too that the institution will either afford student nurses under the plan an opportunity to complete their course of training until graduation and will pay such student nurse a stipend at a monthly rate of not less than $30 for the period following the period of combined study and practice prior to graduation or will transfer such student, after completion of the period of combined study and practice prior to graduation, for training in some other institution. H. R. 2330, introduced by Representative Somers, New York, would authorize an appropriation of $1,500,000 to construct in the borough of Brooklyn, city of New York, a modern, fireproof general medical and surgical hospital and domiciliary facility for the care and treatment of veterans, with a capacity of at least 500 beds.

STATE MEDICAL LEGISLATION

Kansas

Bills Enacted.—S. Res. 25 was adopted, March 12. It directs the legislative council to study the advisability and necessity for the inclusion in the benefits of the workmen's compensation act of workmen suffering from occupational diseases and further directs that the council make a report of its study at the next regular session of the legislature, together with such recommendations as it may see fit to adopt. H. 332 was approved, March 22. It requires every physician to take or cause to be taken a sample of blood of any woman whom he diagnoses as being pregnant, such sample to be taken within fourteen days after the diagnosis is made.

Maine

Bill Introduced.—H. 632, to amend the premarital examination law, was amended in the house by eliminating therefrom the provision authorizing a doctor of the armed forces of the United States to execute the required certificate.

Bill Enacted.—S. 304 has become chapter 155 of the Public Laws of 1943. It amends the osteopathic practice act by authorizing approved osteopathic schools to give a course of instruction for a total of thirty-six months within a three to four year period when such school has adopted compressed or accelerated courses as a war emergency measure.

Maryland

Bill Introduced.—H. 644 proposes certain regulations concerning advertising by persons practicing medicine and surgery.

Michigan

Bills Enacted.—S. 113 has become Public Acts No. 33 of the Acts of 1943. It amends the medical practice act by authorizing the Michigan state board of registration in medicine to suspend in whole or in part the educational requirements prescribed by the act at any time during the state of war now existing between the United States and various other nations. S. 192 has become Public Act No. 44 of the Acts of 1943. It amends the osteopathic law by authorizing the Michigan state board of osteopathic registration and examination to modify, by order, the educational requirements prescribed by the present act, during the present emergency.

Minnesota

Bill Introduced.—S. 1079 proposes the creation of a committee, at least two members of which shall be doctors of medicine appointed by the council of the Minnesota State Medical Association, for the purpose of establishing standards and prescribing scientifically approved methods to secure the selection of children with an impaired sense of hearing and to institute an educational program for the prompt medical correction thereof.

Missouri

Bills Introduced.—S. 79 proposes a new law to be known as the Missouri Food, Drug and Cosmetic Act. Among other things, it proposes that a drug shall be deemed misbranded if it is sold at retail and contains any quantity of aminopyrine, barbituric acid, cinchophen, dinitrophenol, sulfanilamide, or their derivatives, or any other drug which has been found by the board to be dangerous to health when used in the dosage or with the frequency or duration prescribed, recommended or suggested in the label thereof, unless such drug is sold on a written prescription signed by a licensed physician, dentist or veterinarian, and its label bears the name and place of business of the seller, the serial number and date of such prescription, and the name of such physician, dentist or veterinarian. When sold on such written prescription such drug shall be exempt from the other provisions of the proposal. S. 98 proposes the creation of a state board of examiners in the basic sciences to examine, in the subjects of anatomy, physiology, chemistry, bacteriology and pathology, all applicants for a license to practice any form of the healing art.

Nebraska

Bills Enacted.—Bill No. 40 was approved, March 27. It requires each applicant for a marriage license to present a certificate signed by a duly qualified physician licensed to practice medicine and surgery in any state or United States territory, or any other person authorized by the laws of Nebraska to make such certificate, certifying that the applicant is not infected with syphilis in a communicable stage. Bill No. 41 was approved, March 27. It requires every physician, or other person authorized by law to practice obstetrics, attending a pregnant woman to take a sample of blood of such woman at the first examination and submit such sample to an approved laboratory for a standard serologic test for syphilis.

Nevada

Bill Enacted.—A. 141 was approved, March 20. It authorizes the board of medical examiners to grant qualified physicians a temporary license to practice medicine, surgery or obstetrics in any particularly specified part of the state for and during the period of time limited by the license. The law further authorizes the board of medical examiners, from time to time, to restrict, enlarge or change the territorial limits stated in such temporary license.

New Jersey

Bills Introduced.—S. 95 proposes the establishment of an elective system of compensation for silicosis and asbestosis. S. 143 proposes to authorize the state department of health to require a person suspected of suffering from a communicable disease, or suspected of being a carrier of such disease, to submit to a medical examination made by a physician or laboratory selected by the state department of health or the local board of health. S. 158 proposes the establishment within the department of institutions and agencies of a division whose duty it shall be to study the causes, mortality rate, treatment, prevention and cure of cancer and allied diseases and proposes to authorize the department to make a careful study of the cancer situation in the state, organize cancer clinics at various points throughout the state, conduct a program of public education regarding the care, treatment and prevention of cancer and erect and maintain a state hospital wherein cancer patients may be received for care and treatment.

Bill Enacted.—A. 93 has become chapter 17 of the Laws of 1943. It amends the medical practice act by granting an extension of two years within which a licentiate must furnish proof of his actually having become a citizen.

New York

Bills Passed.—A. 335 passed the assembly on March 16 and the senate on March 17. It proposes to authorize the state commissioner of health to employ necessary medical and health personnel for rendering services in areas designated by the governor as being emergency health and sanitation areas by virtue of an inadequacy of medical facilities or personnel therein. Compensation to such employed medical personnel may be paid by the state department of health. A. 1923 passed the assembly on March 24 and the Senate on March 26. To amend the mental hygiene law, it proposes to eliminate the existing requirement that the head of the department be a reputable physician with at least ten years' experience in the actual practice of his profession and at least five years' actual experience in the care and treatment of persons afflicted with mental disease in an institution for their care and treatment. It then proposes to provide for the appointment of a medical director who shall be a reputable physician, a graduate of an incorporated medical college, with at least ten years' experience in the actual practice of his profession and at least five years' actual experience in the care and treatment of persons afflicted with mental disease in an institution for their care and treatment. The duties of the proposed medical director would be to advise with the commissioner on all matters affecting medical policy within the department, have direct charge and control, under the general departmental direction of the commissioner, of medical administration, care and treatment, and of medical and nursing personnel, and perform such other duties in the place and stead of the commissioner as may lawfully be assigned to him.

North Carolina

Bills Enacted.—S. 211 was ratified, March 6. It amends the law relating to the incorporation of nonprofit hospital service corporations so as to authorize the operation of nonprofit medical service plans as well. The term "hospital service plan" is defined as including the contracting for hospital care, laboratory facilities, x-ray facilities, drugs, appliances, anesthesia, nursing care, operating and obstetric equipment, accommodations and any other services authorized or permitted to be furnished by a hospital under the laws of North Carolina and approved by the North Carolina Hospital Association or the American Medical Association. The term "medical service plan" is defined as including the contracting for medical, obstetric, surgical and any other professional services authorized to be furnished by a duly licensed physician. S. 254 was ratified, March 10. It authorizes the creation of a Hospital Authority to engage in hospital construction, maintenance and operation. H. 174 was approved, February 15. It amends the law relating to the disposition of dead bodies by, among other things, making available for distribution to medical schools for dissection purposes, by the Board of Anatomy, the bodies of Confederate soldiers and of soldiers, sailors and marines of the World War and their wives. Such bodies were not available under the prior law.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ARIZONA

State Medical Meeting.—The fifty-second annual meeting of the Arizona State Medical Association will be held at the Pioneer Hotel, Tucson, April 30-May 1, under the presidency of Dr. E. Payne Palmer, Phoenix. The preliminary program includes the following speakers:

Dr. Clarence E. Rees, San Diego, Calif., A New Method of Tendon Suture.
Dr. Charles S. Kibler, Tucson, Demonstration of Heart Disease.
Dr. Adrian E. Clark, Globe, A Case of Banti's Disease with Apparent Recovery.
Dr. E. Henry Running, Phoenix, Vomiting During the First Few Days of Life.
Dr. Melvin L. Kent, Mesa, Intractable Glossitis—Report of a Case.
Dr. James M. Ovens, Phoenix, Herniated Intervertebral Disk, Diagnosis and Treatment.
Dr. Archie P. Kimball, Yuma, An Outline of the Medical and Surgical Aspects of Commonly Used Sulfonamides.
Dr. James Lytton-Smith, Phoenix, Common Errors of Orthopedic Surgery.
Dr. Howard C. James, Tucson, Maternal Deaths.
Dr. Alexander N. Shoun, Benson, Rheumatic Heart Disease in Arizona.
Dr. Paul Henry Case, Phoenix, Recent Advances in Ophthalmology of Interest to the General Practitioner.
Dr. Charles A. Thomas, Tucson, Collapse Therapy for the Treatment of Tuberculosis in Patients of Advanced Years.
Dr. Archie E. Cruthirds, Phoenix, A Brief Summary of the Present Treatment of Chronic Sinusitis.
Dr. Philip H. Loveless, Morenci, A Case of Abdominal Pregnancy.
Dr. Earle W. Phillips, Phoenix, Relief of Allergic Premenstrual Headache.
Dr. Victor S. Randolph, Phoenix, Results of Thoracoplasty—A Five and Ten Year Study.

CALIFORNIA

Court Nullifies Revocation of License.—A writ of mandate, issued by the San Francisco Superior Court, nullifying the revocation of the license of Dr. George C. H. McPheeters, Fresno, by the state board of medical examiners, has been entered in the medical register in the Fresno County clerk's office, newspapers reported February 6. Dr. McPheeters' license to practice was revoked by the state board Oct. 21, 1942, following a hearing in Sacramento in which he was said to have been found guilty of offering to procure an abortion.

Increase in Infant Mortality.—With 21 infant deaths reported for the week ended March 13, the San Francisco Department of Public Health announces a new high in infant mortality. This group brings the total for the first ten weeks of the year to 120 infant deaths under 1 year; 50 for January, 38 for February and 32 for the first two weeks of March. The department points out that of the 120 deaths, 27 were among nonresidents of the city and county of San Francisco. Fifteen of the group of infants died from enteritis (under 2 years) and 10 of congenital heart disease. Thirty-four deaths were attributed to prematurity.

FLORIDA

Personal.—Dr. Henry E. Palmer, Tallahassee, was guest of honor at a dinner recently in recognition of his completion of fifty years in the practice of medicine.——Dr. Elijah Thomas Sellers, Jacksonville, was recently guest of honor at a gathering given to celebrate his fifty-sixth birthday. Dr. Robert B. McIver, Jacksonville, was host to the one hundred and seventy-five physicians who attended.——Dr. Noble A. Upchurch, who has been health officer of Jacksonville since 1925, resigned January 1 on account of ill health. He has been succeeded by Dr. Wieland W. Rogers, who has been connected with the department for about fourteen years.——Dr. P. T. McClellan was recently appointed health officer of Vero Beach.

Resolution on Temporary Licenses.—The Lake County Medical Society on March 4 expressed its opposition to the licensing of or granting temporary permits to physicians who have not provided themselves with licenses through the regular channels provided by the state laws, except in counties in which there is an actual shortage of physicians. The society recommended that the county medical society in that county in which "emergency exists" shall request that a temporary permit be granted to physicians who have not provided themselves for licenses through the regular state channels. The resolution adopted by the society urged that such temporary permits be terminated at the end of the present emergency. The society expressed its agreement with the state board of medical examiners in its effort to protect the interests of Florida licensed physicians both at home and in the armed forces.

NEVADA

New Secretary of State Association.—Dr. Moreton J. Thorpe, Reno, has been appointed secretary of the Nevada State Medical Association to succeed Dr. Roland W. Stahr, Reno, who has been called to active military duty. Dr. Thorpe graduated at the University of California Medical School, San Francisco, in 1932.

NEW HAMPSHIRE

Personal.—Dr. Gene B. Haber, formerly of Philadelphia, U. S. Public Health Service, was recently assigned as health officer of the Eastern District of the New Hampshire State Board of Health with headquarters at Exeter. He succeeds Dr. Edward W. Colby, who is now in charge of the division of epidemiology of the state board of health at Concord.

Name of Department of Health Changed.—Under the terms of a recently enacted law which becomes effective on July 1 the state board of health is, for administrative purposes, to be officially known as the "State Department of Health of New Hampshire." The title of the executive officer will be state health officer instead of secretary as in the past. The act also prescribes that the latter, who also serves as secretary to the board, "shall be a physician and a person with knowledge of and experience in public health work and sanitary science . . . and shall be the registrar of vital statistics of the state." As in the past, the board is composed of the governor and the attorney general as ex officio members and with five others, of whom three are physicians, one a civil engineer and one who is "neither a physician nor a civil engineer" (the latter at the present time a pharmacist). According to *New Hampshire Health News* a new division of diagnostic laboratories is now located at the state hospital, Concord.

NEW JERSEY

Dr. John Baker Lectures for Cereal Chemists.—John C. Baker, Ph.D., chief chemist of Wallace & Tiernan Company, Inc., Newark, was chosen by the American Association of Cereal Chemists to lecture throughout the country on "Gluten and Its Relation to Flour Constituents in Bread Making." Dr. Baker spoke in Columbus, Ohio, March 27; Fort Worth, Texas, March 31; Manhattan, Kan., April 3; Winnipeg, Canada, April 5; Minneapolis, April 7, and Chicago, April 9. This is the second year that the American Association of Cereal Chemists has chosen one of its members to lecture to its sections throughout the country on special research work.

NEW YORK

County Society Votes to Bar Alien Physicians.—The Erie County Medical Society recently unanimously voted to bar from its membership "physicians who are not United States citizens." The action was taken "to protect the postwar interests of the physicians called to war," it was reported.

Amebic Dysentery at State Hospital.—An investigation is under way at Creedmoor State Hospital, Queens Village, to determine the cause of an outbreak of amebic dysentery. Since last June 97 cases have occurred. Of this number 16 patients and 6 employees had been "clinically sick," with 11 employees and 26 patients mildly affected, newspapers reported. In addition, 38 "carriers" of the organism were found. On March 18 only 1 person at the hospital was actually ill with the disease, although 35 to 40 patients and employees were still isolated.

New York City

Personal.—Dr. Howard Fox has been appointed consultant in tropical medicine to the Secretary of War.——Dr. Thomas A. Gonzales, chief medical examiner of the City of New York, has been made an honorary member of the Asociacion Medica Argentina.

Physicians' Orchestra Suspends Activities.—The Doctors Musical Society of Brooklyn has been compelled to suspend activities for the duration because of the loss of many of its members to the armed services.

Missing in Action.—Capt. A. Leonard Hymes, M. C., Army of the United States, Brooklyn, while on active duty with the air corps somewhere in the South Pacific has been reported missing in the service of his country. Captain Hymes graduated at the New York University College of Medicine in 1939.

The First Béla Schick Lecture.—Dr. William E. Ladd, professor of child surgery, Harvard Medical School, Boston, will deliver the first Béla Schick Lecture at Mount Sinai Hospital, April 13. His subject will be "Time and Choice of Operation in Early Life." The lecture is one of a series planned in honor of Dr. Béla Schick, now consultant and formerly pediatrician in chief at the Mount Sinai Hospital and is made possible by a fund contributed in 1942 by friends and associates of Dr. Schick.

OHIO

Missing in Action.—Lieut. Aaron S. Michelson, Cincinnati, medical officer of the destroyer U. S. S. *Laffey*, has been officially reported missing. The *Laffey* was one of seven U. S. destroyers lost in an engagement at Guadalcanal. Press reports indicate that Lieutenant Michelson was trapped below deck while helping remove wounded sailors from the doomed vessel. Before entering the Navy in May 1942, he had been chief resident at the Jewish Hospital, Cincinnati, and assistant clinician in general medicine at the Cincinnati General Hospital.

Personal.—William S. Keller, senior surgeon, U. S. Public Health Service Reserve, regional medical officer, Fifth Civilian Defense Region, Cleveland, recently bestowed a citation on Dr. Clyde M. Fitch, chief of emergency medical service in Portsmouth, and Dr. Orville J. Walker, chief of emergency service in Youngstown, for "outstanding accomplishments and efficiency in organizing" the civilian defense setup.——Dr. Irvin Abell, Louisville, Ky., was presented with an honorary degree of doctor of laws during the recent annual commencement of the University of Cincinnati College of Medicine.

Institute of Medical Research Dedicated.—The Institute of Medical Research at the Toledo Hospital, Toledo, was dedicated on March 27. The institute is housed in a new two story building made possible by an endowment from the late Frank Collins of the National Supply Company, Toledo. The staff includes a biochemist, nutritionist, bacteriologist, pathologist and biophotographer under the direction of Dr. Bernhard Steinberg, Toledo. The staff will be augmented by a physiologist, biophysicist and pharmacologist. Provision has been made to accept fellows in medical and dental research. The institute will not be devoted to the study of a single disease but will maintain interest in diseases in general, depending on the availability of the personnel. Dr. Cyrus C. Sturgis, professor of internal medicine and director of the Thomas Henry Simpson Memorial Institute for Medical Research, University of Michigan Medical School, Ann Arbor, gave the dedicatory address on "The Future of Medical Research." Other speakers included Frank Adams, chairman of the research board, Reverend Russell J. Humbert, pastor of the Epworth Methodist Church, and the Honorable Lloyd Roulet, mayor of Toledo.

PENNSYLVANIA

Society News.—Dr. Benjamin H. Shuster, Philadelphia, discussed vertigo before the Reading Eye, Ear, Nose and Throat Society recently. At a meeting of the Fayette County Medical Society in Uniontown, April 1, Dr. Joseph V. Marnell spoke on diagnosis and management of deep neck infections.

Philadelphia

Committee on Physicians' Health.—The Commission of Physicians' Health of the Philadelphia County Medical Society has been temporarily disbanded because of the number of physicians in the vicinity who are in the armed forces and the death of the chairman of the commission, Dr. James Alexander Clarke Jr. One of the commission's principal objectives was to carry out periodic health examinations of members of the society.

Annual Postgraduate Institute.—The Philadelphia County Medical Society will hold its eighth annual postgraduate institute at the Benjamin Franklin Hotel, May 11-14. About seventy speakers will participate, their presentations covering a wide range of medical subjects. On Monday evening, May 10, a joint meeting of the Philadelphia Health Association and the section on medicine of the Philadelphia College of Physicians will be addressed, among others, by Dr. Clarence E. de La Chapelle, New York, on the "Treatment of Coronary Thrombosis."

Herbert Fox Memorial Fellowship.—David L. Coffin, D.V.M., instructor in veterinary pathology at the University of Pennsylvania, has been appointed to the Herbert Fox Memorial Fellowship in comparative pathology at the Zoological Society of Philadelphia. Dr. Coffin, who is the first incumbent of the fellowship, will serve as assistant to Herbert L. Ratcliffe, Sc.D., recently appointed director of the Penrose Research Laboratory of the Zoological Society and assistant professor of comparative pathology at the University of Pennsylvania. The fellowship was established in 1942 by the Zoological Society in memory of Dr. Herbert Fox, pathologist and director of the Penrose Laboratory from 1907 to 1942 and professor of comparative pathology at the university from 1927 to 1942. It provides for half time work at the Zoological Garden by faculty members of the School of Veterinary Medicine of the university who are interested in the diseases of wild animals.

Pittsburgh

Hospital News.—A new addition to St. Joseph's Hospital and Dispensary costing $500,000 was opened on March 19. The new unit offers advanced facilities for the treatment of pediatric, gynecologic and maternity patients as well as for general and special x-ray diagnosis and therapy. The hospital, with the new addition, now has a capacity of 250 beds.

Society News.—The Pittsburgh Surgical Society was addressed, March 25, by Drs. Theodore S. Swan on "Surgical Aspects of Diverticulitis"; William S. McEllroy, dean of the University of Pittsburgh School of Medicine, "Effect of the Army and Navy Collegiate Program on Medical Education," and Herbert Frankenstein, "Acute Inflammation of the Appendices Epiploicae."

VERMONT

New Blood Bank at Medical School.—A blood plasma bank was formally opened on March 19 in space provided by the University of Vermont College of Medicine, Burlington. The bank is a cooperative one in which the state contributed $3,000 of the $30,000 which was collected in a statewide campaign. Dr. Wendell E. James, associate professor of bacteriology and clinical pathology at the school, is director of the bank and processing laboratory. There are fourteen hospitals in the state that are cooperating and the bleeding is to be done at these hospitals, the donors registering with the local Red Cross agencies. The blood is to be shipped to the laboratory for processing, and each hospital is allocated 1 unit for each bed until the total bank reaches 2,000 units. Plasma will be available not only for civil defense but for civilian needs also, and if, as is expected, there is a surplus above this point, it will be donated to the military service.

VIRGINIA

Stuart McGuire Lectures.—Dr. Philip D. Wilson, clinical professor of orthopedic surgery, Columbia University College of Physicians and Surgeons, New York, gave the fourteenth annual Stuart McGuire Lectures at the Medical College of Virginia, Richmond, February 25-26, on "The Treatment of War Injuries, Especially Compound Fractures" and "Amputations in Wartime." The lectures were given in conjunction with the spring postgraduate clinic, consisting this year of a symposium on low back pain. Speakers in the symposium included Dr. Emil J. C. Hildenbrand, associate professor of clinical surgery, Georgetown University School of Medicine, Washington, D. C., from the point of view of the physical therapist, and the following physicians from the staff of the medical school: Drs. Henry Page Mauck, professor of clinical orthopedic surgery; Claude C. Coleman, professor of neurologic surgery; James Asa Shield, assistant professor of neuropsychiatry, and Randolph H. Hoge, assistant professor of gynecology.

WEST VIRGINIA

Medical Consultant for Bureau of Hygiene.—Dr. Henry M. Brown, industrial physician at the du Pont plant at Belle, has been appointed medical consultant for the bureau of industrial hygiene of the West Virginia State Department of Health. While he has been appointed to succeed Dr. John W. Crosson, who was director of the bureau until his resignation to become industrial consultant for Sharp & Dohme, Philadelphia, Dr. Brown will serve in a consulting capacity only.

Personal.—Norman H. Baker, D.D.S., Charleston, has been reappointed as the dental member of the Public Health Council of West Virginia, for the term ending June 30, 1945.——Dr. Benjamin E. Hodge, Clarksburg, representing the West Virginia State Medical Association, has been appointed a member of the West Virginia State Nutrition Committee, succeeding Dr. James Lewis Blanton, Fairmont, who has entered the U. S. Army Medical Corps.——Dr. Erlond H. Hedrick has been appointed medical superintendent of Pinecrest Sanitarium, Beckley, succeeding Dr. Kyle M. Jarrell, who had held the position since 1933.

Committee to Study Medical Care and Hospital Service.—A fact finding and planning committee has been appointed by Dr. Robert J. Wilkinson, Huntington, president of the state medical association, to study prepayment plans

providing medical care and hospital service. The appointment of the committee followed the recent passage of a bill providing for the operation of hospital service plans in West Virginia. The bill is effective only until Feb. 28, 1945, and the new committee will endeavor to draft a bill for introduction to the next session of the legislature that meets with the approval of the medical profession and hospitals in West Virginia. The committee will also study the possibility of establishing a full time trained health personnel for every county or group of counties in the state, the treatment and control of tuberculosis, together with the problem of handling tuberculous patients, and the management of state tuberculosis sanatoriums and hospitals for the treatment of mental diseases. Members of the new committee are Drs. Ray M. Bobbitt, Huntington, chairman; Delivan A. MacGregor, Wheeling; Thomas L. Harris, Parkersburg; John P. Helmick, Fairmont; Frank V. Langfitt, Clarksburg; Carl E. Johnson, Morgantown; Frank J. Holroyd, Princeton; Benjamin H. Swint, Charleston, and Hu C. Myers, Philippi.

GENERAL

Meetings Canceled.—The American Society for Clinical Investigation has canceled its thirty-fifth annual meeting, which was scheduled for Atlantic City, May 3.——The Association of American Physicians has canceled its annual meeting scheduled for Atlantic City, N. J., May 4-5.

Seek Apprehension of Male Nurse.—Robert Edward White, nurse and ex-convict, is wanted by the San Francisco Police Department because of an alleged theft of $1,400 from

Robert Edward White

a patient. White disappeared and, according to Charles W. Dullea, chief of police of San Francisco, is expected to seek employment in a hospital as soon as the money is gone. His social security number is 526-22-9810. He is 42 years old, 5 feet 5½ inches tall, weighing 150 pounds, and has blue eyes and brown bushy hair. A peculiarity is that his eyebrows run across his nose. He is a native of Missouri. Any one recognizing this man is urged to communicate with the local police department immediately.

Lilly Prize Awarded to Dr. Carter.—Herbert E. Carter, Ph.D., assistant professor of chemistry, University of Illinois, Urbana, will be presented with the $1,000 Eli Lilly & Co. Prize in biological chemistry for 1943 at the annual meeting of the American Chemical Society, Detroit, April 14. Dr. Carter, who is 32 years of age, was awarded the prize in recognition of his studies on amino acids, the building blocks of proteins and of fatty acids.

The Interne Continues Publication.—The Association of Internes and Medical Students announces that despite a rapidly changing staff the *Interne*, the official journal of the association, will continue publication, featuring articles on the armed services and other aspects of the war effort which are of particular interest to medical students and physicians. The present staff includes Dr. Jerome M. Schneck and Nathaniel Gottesman, editors; Dr. Kenneth L. Zierler, Baltimore, features; Dr. John L. Simon, Brooklyn, books; Dr. Leon N. Greene, New York, humor, and Mr. Julian Farren, managing editor. Communications should be addressed to Dr. Schneck, 40 East Tenth Street, New York.

CANADA

Woman Graduate Honored.—Dr. Augusta Stowe Gullen, Toronto, Ont., reported in the *Canadian Medical Association Journal* as the first woman to obtain her medical degree from a Canadian university, was recently paid special tribute in recognition of her sixtieth anniversary of graduation from medical school. Dr. Gullen's mother, Dr. Emily Howard Jennings Stowe, was the first woman to practice medicine in Canada, but she obtained her degree in New York, according to the Canadian journal. At the opening of the Ontario Medical College for Women, Toronto, Dr. Gullen was appointed demonstrator of anatomy, later lecturer on children's diseases and subsequently professor of pediatrics, a position she held until the women's medical college was amalgamated with the University of Toronto. She served in the senate of the University of Toronto from 1910 to 1922.

Canadian Association Holds Special Meeting of Council.—For the first time, the council of the Canadian Medical Association called a special meeting, January 18-19, to discuss health insurance and other urgent matters under consideration by the executive committee. Unanimous approval was given to a resolution that the association adopt the principle of health insurance, favoring a plan "which will secure the development and provision of the highest standard of health services, preventive and curative, if such plan be fair both to the insured and to all those rendering the services." At this meeting a report of the department of cancer control was submitted which urged that cancer be made a reportable disease in the Dominion and the appointment of a commission whose responsibilities would be to correlate all data incident to cancer for educational and statistical purposes, to establish cancer treatment centers, to administer all grants, gifts and bequests for cancer work, to concern itself with the problem of the transportation of patients who live at a distance from a treatment center and to foster research in cancer. The association decided to let its annual meeting in Montreal take the form of a business meeting; the executive committee will meet, June 12-13, and the general council, June 14-15.

Deaths in Other Countries

Major General Amin Fahd Maluf Pasha, M.D., formerly principal medical officer of the Iraq army, died at his home in Heliopolis, Egypt, on January 21 in his seventy-first year. He began his career in military medicine as an officer in the Egyptian army and served a few years in the Sudan. On the Arabian revolt in the last war he resigned his position in the Egyptian army and joined King Feisal's troops as a surgeon. He was decorated ten times. A graduate of the American University Beirut, Major General Maluf was elevated from a colonelcy and created a pasha on his retirement about fifteen years ago. His latest works are "An Arabic Zoological Dictionary" and "An Astronomical Glossary."

Government Services

Dr. Sherman Heads Bureau of Human Nutrition

Henry C. Sherman, Sc.D., Mitchill professor of chemistry, Columbia University, New York, has been appointed head of the newly established bureau of human nutrition and home economics of the United States Department of Agriculture, Washington, D. C. Dr. Sherman has been at Columbia University since 1897.

Dr. DeLien Named Assistant in Office of Indian Affairs

Dr. Horace DeLien, special expert in tuberculosis in the Office of Indian Affairs, has been appointed assistant to the director of health, Dr. John R. McGibony, Chicago, succeeding Dr. Lawrence W. White, Chicago. Dr. DeLien graduated at the University of Minnesota Medical School, Minneapolis, in 1933, and engaged in private practice in Mobridge, S. D., for several years. Prior to entering the Indian Service in 1938 he was director of the Pennington County Health Unit in South Dakota, with headquarters in Rapid City. In 1941 he was transferred from his work as special physician in tuberculosis control of the Indian Service for California, Nevada and Utah to additional responsibilities as special expert in tuberculosis.

Foreign Letters

SWITZERLAND

(From Our Regular Correspondent)

Feb. 20, 1943.

Nutrition of Infants and Children in Wartime

The nutrition of infants and children in wartime was discussed at the latest meeting of the Swiss Society of Pediatrics. On the basis of the papers read the resolutions stressed the importance of breast milk for nurslings. Adults can live without milk, children cannot. All milk products are to be reserved for infants and patients, and their sale to other persons is to be prohibited. A ration card for infants and a similar one for children to the end of the fifth year of life were proposed. They provide the following:

(*a*) A rationing card for infants which is to be used to the end of the first year of life:

	Per Day	Per Month
Milk	660 Gm.	20 liters
Sugar	40 Gm.	1,200 Gm.
Rice	20 Gm.	600 Gm.
Grits	20 Gm.	600 Gm.
Flour	20 Gm.	600 Gm.
Butter	10 Gm.	300 Gm.
Cheese	5 Gm.	150 Gm.
Cocoa or tea	.....	100 points
Eggs	.....	2

(*b*) A ration card for children, which is to be used to the end of the calendar year in which the child completes its fifth year:

	Per Month
Farinaceous foods	
Rice, oats or barley	750 Gm.
Flour, grits, maize	750 Gm.
Baked foods	250 Gm.
Bread	4,500 to 6,000 Gm.
Sugar	1,000 Gm.
Milk	20 liters
Oil or fat	100 Gm.
Butter	400 Gm.
Potatoes	4,500 Gm.
Cheese	150 Gm.
Meat	500 Gm.
Legumes	100 Gm.
Eggs	4
Cocoa or chocolate	200 points

Lactic acid is to be reserved for the preparation of lactic acid milk for nurslings and for the preparation of lactic acid powdered milk.

Pediatricians have lodged a complaint regarding the advertising methods of manufacturers of special food preparations for children. The pediatric society passed a resolution which objected to the practice of certain producers of special nutrient substances for children. The resolution points out that their propaganda methods are no longer compatible with the welfare of the population in general. It is intolerable that representatives of these manufacturers or children's nurses who have been hired for the purpose, urge mothers to depart from the food formulas prescribed by physicians and use their canned products instead.

Swiss pediatricians emphatically object that physicians or the editors of periodicals who point out that the healthy child does not need special nutritional preparations and that they represent an unnecessary increase in food costs are called to account by these manufacturers of special nutrient substances and are threatened with legal and economic reprisals.

Swiss pediatricians are of the opinion that manufacturers of nutrient substances are not dependent on such methods of advertising and therefore urge these firms to refrain from this practice.

Feeding of Patients Under Swiss Food Rationing

A committee for war nutrition has existed in Switzerland since the beginning of the war. Prof. Dr. Alfred Fleisch, physiologist of the University of Lausanne, is its president. This committee has formulated guiding principles for physicians on the feeding of patients under food rationing. In October 1942 new regulations became necessary because the food supply of the country had taken an unfavorable turn and a number of new measures became necessary; for instance, bread and milk had to be included in the rationing. Whereas formerly 3,000 calories was regarded as a basis for the daily requirements, it became necessary to reduce it to 2,400 calories (protein 80 Gm., fat 55 Gm. and carbohydrates 400 Gm.). Additions can be granted only if the health of a person makes this absolutely essential. Excessive special grants may jeopardize the entire food balance of the country. Instead of computing optimum figures, the physician must now consider minimum figures.

Exact regulations have been formulated with regard to permits for additional rations by physicians. These are based as far as possible on the principle of compensation; that is, one food is exchanged against another one that is more suitable in the particular disorder. The measures to effect savings go so far that for bedfast patients from 1,800 to 2,000 calories is estimated as adequate. Only patients with prolonged disorders are entitled to special rations. For short illnesses, rations are not usually granted. Convalescents likewise are not entitled to special rations. Only five groups of patients are to receive special rations: those with gastrointestinal disorders, diabetes, hepaticobiliary disorders, renal diseases and tuberculosis. In other types of disorders, special rations are to be granted only in exceptional cases. Officially approved physicians are to make the decisions regarding requests for special rations. A detailed table has been made up to estimate rations for patients, and this table has been further amplified by special regulations. These amplifications are concerned with the granting of eggs instead of meat, with nutritive preparations, children's foods, coffee, tea, cocoa, honey, and oils and fats for medical purposes. Other regulations are concerned with the consumption of meat on meatless days, special rations for blood donors, white bread for persons with gastrointestinal disorders, children's rations, sweetening substances for diabetic patients, and so on. All this indicates that in Switzerland it has become necessary to introduce extreme restrictions even as regards patients.

Porphyrins in the Healing of Wounds

Prof. Dr. Emil Buergi of Bern discussed the use of porphyrins in the healing of wounds in the Medical Society of Bern on the basis of observations made in the Pharmacologic Institute, of which he is the head. The porphyrin ring develops when four pyrroles are linked together by CH groups. Depending on whether the free valences of the N atoms in the ring are replaced by iron or magnesium there develops blood pigment, chlorhemin or chlorophyll.

The tonicizing and wound healing action of the porphyrins was studied in 300 rabbits, in which two pieces of skin were cut out on symmetrical sites of the back. The defects were subjected to comparative treatment by prophyrin ointments, pure ointment bases and other ointments. The efficacy of the examined substances could be estimated only on the basis of rapidity and perfection of the resulting regeneration, because every wound left to itself heals automatically. Furthermore, individual differences in the reaction capacity of the individual animals had to be considered.

Studies were made on chlorophyll, blood pigments and muscle porphyrins. The raw chlorophylls, the pure extracts as well as the water soluble chlorophyll sodium, which contain magnesium in the porphyrin ring, have an excellent curative effect on

wounds. Other plant pigments such as carotene and vitamin A have only a slight effect, and riboflavin and vitamin C have no influence at all.

The blood pigments exert the same effect on wounds as does chlorophyll. However, it is peculiar and unexplainable that the nonferric derivatives of hemoglobin, hematoprophyrin and even bilirubin have a noticeable healing effect on wounds, whereas phenophytin, which is free of magnesium, has no effect whatever. The muscular porphyrins and muscular pulp were found extremely effective. The porphyrins greatly stimulate the formation of granulations, but they influence epithelization only slightly. Their toxicity is negligible. A disinfecting action of the porphyrins could not be ascertained, in contradistinction to the observation of the American Gruskin.

BRAZIL

(From Our Regular Correspondent)

March 17, 1943.

Vital Statistics of Rio de Janeiro

Provisional vital statistics for the city of Rio de Janeiro for the year 1942 are now available. The figures may be compared to those for 1941 (THE JOURNAL, May 2, 1942, p. 96). The population of the city as of July 1, 1942 was 1,853,264. The number of deaths from all causes was 32,502, giving an annual crude death rate of 17.54 per thousand of population, which is slightly lower than that of the previous year (17.89) and that of the average for the five year period 1937-1941 (17.60). The number of live births registered was 39,211, giving a birth rate of 21.15, which is a much better figure than that of the previous year (19.28). The vital index was 121, an improvement over the 1941 figure (108). The number of deaths in the age group 0-1 year was 6,015, which corresponds to the high rate of 153 infant deaths per thousand live births, nevertheless a little better than the rate for the previous year (180). The fetal mortality was 77.73 per thousand total births, as 3,304 stillbirths have been registered. The number of deaths from causes related to pregnancy, childbirth and the puerperium was 304, corresponding to a maternal mortality rate of 7.75 deaths per thousand live births, or 1 maternal death in 129 live births.

First as a cause of death are "all forms of tuberculosis," with a total of 5,773 deaths (5,606 from tuberculosis of the respiratory apparatus), or 17.76 per cent of the total of deaths from all causes—a crude specific death rate of 312 per hundred thousand of population as against 316 in the previous year. Tuberculosis is still a very important problem of the city in spite of the efforts made by the health department in the past years. The rest of the "infectious and parasitic diseases" caused 4,571 deaths, which, with the deaths from tuberculosis, gives a total of 10,344 deaths from infectious and parasitic diseases (31.83 per cent of the deaths from all causes). Of this total 116 were from typhoid, which corresponds to an annual death rate of 6.26 per hundred thousand, against 7.17 in 1941 and 7.10 in the five year period 1937-1941. The other principal infections were dysentery, mainly bacillary, with 334 deaths (18.02 per hundred thousand), measles with 322 deaths (17.37 per hundred thousand), whooping cough with 277 deaths (14.95 per hundred thousand), diphtheria with 143 deaths (7.72 per hundred thousand), malaria with 195 deaths (10.52 per hundred thousand), influenza with 1,222 deaths (65.94 per hundred thousand), leprosy with 52 deaths (2.81 per hundred thousand) and poliomyelitis with 3 deaths (0.16 per hundred thousand). Tetanus (about 50 per cent umbilical) caused 210 deaths (11.33 per hundred thousand). The annual death rates from these infections for 1941 and for the five year period 1937-1941 were, respectively, dysentery 14.06 and 14.40 per hundred thousand, measles 12.02 and 14.61, whooping cough 15.60 and 15.42, diphtheria 10.59 and 8.41, malaria 12.07 and 12.50, influenza 60.65 and 55.30, leprosy 3.14 and 3.62, poliomyelitis 0.05 and 0.41 and tetanus 11.69 and 10.11. In 1942 cancer caused 1,248 deaths, or 67.34 per hundred thousand (66.44 in 1941), thus being on a continuous increase since 1903-1907, when the mean annual crude death rate was 34.75.

The second most important single group of causes of death is that of the diseases of the circulatory system, represented by a total of 5,717 deaths, or 17.59 per cent of the deaths from all causes, which corresponds to the rate of 308 per hundred thousand (308 in 1941). Out of this total 4,533 deaths have been reported as due to diseases of the heart, which corresponds to the rate of 245 per hundred thousand (217 per hundred thousand in 1941). This represents a new increase in the number of deaths from diseases of the heart. The crude annual specific death rate from diseases of the cardiovascular system is on a rapid increase in Rio de Janeiro, as clearly shown by these figures: 178 in 1932-1936, 235 in 1937-1941 and 308 in 1942.

The third leading group of causes of death is that of the diseases of the digestive apparatus, represented by 5,139 deaths, or 15.81 per cent of the deaths from all causes, which corresponds to the rate of 277 deaths per hundred thousand of population (275 in 1941). The bulk of these deaths is reported under the title of "diarrhea and enteritis under 2 years" (3,573 deaths), which is the largest contribution to the infant mortality; an average of 39 per cent of the infant deaths in Rio de Janeiro are classified as due to diarrheal diseases. The number of deaths registered as caused by appendicitis was 99 (102 in 1941), and that caused by diseases of the liver and the biliary ducts was 409 (418 in 1941), which correspond respectively to 5.34 and 23.63 per hundred thousand of population. The diseases of the nervous system have caused 1,222 deaths, or 65.94 per hundred thousand (71.17 in 1941), the largest contribution being from "intracranial lesions of vascular origin" (876 deaths, or 47.27 per hundred thousand). The total number of deaths registered as caused by diseases of the respiratory apparatus was 3,724, or 11.45 per cent of the total from all causes, and a death rate of 201 per hundred thousand (215 in 1941). The diseases of the genitourinary system have caused 1,431 deaths, or 4.40 per cent of the total from all causes, which corresponds to 77.21 per hundred thousand (74.93 in 1941).

Puerperal septicemia and infection were the cause of 126 deaths, or 41.45 per cent of the maternal deaths (one death in 321 live births as against one in 282 in 1941). Violent deaths were 1,214, or 3.73 per cent of the total of deaths from all causes, which corresponds to the rate of 65.51 per hundred thousand (66.44 in 1941). Out of this total, 198 deaths have been caused by motor vehicle accidents, or 10.68 per hundred thousand, as against 17.92 in 1941, the decrease corresponding to the sharp reduction in automobile traffic due to gas rationing.

Marriages

JOSEPH A. FIORITO, New Haven, Conn., to Miss Edith Patricia Hawley of Montreal, Que., Canada, March 18.

EDWARD GORDON BELL JR., Bronxville, N. Y., to Miss Rose Elizabeth Hynes of New York, March 23.

OMAR FAREED to Mrs. Martha Carr Moon, both of Chicago, in Carson City, Nev., recently.

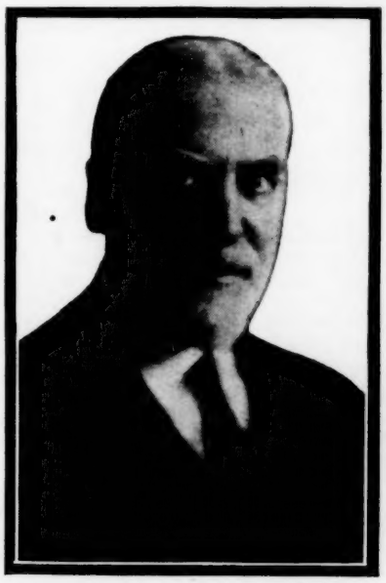
REUBEN LEASS, Framingham, Mass., to Miss Mae Kripke of Boston, March 21.

HARRY E. GRANT, Easton, Ill., to Miss Marietta Crosthwait of Chicago in March.

Deaths

Grant Charles Madill ✠ Ogdensburg, N. Y., long a member of the House of Delegates of the American Medical Association, died, March 26, of myocarditis and cerebral hemorrhage, aged 78. Dr. Madill was born in Stockton, Calif., July 6, 1864. His early education was received at the Ogdensburg Free Academy, Potsdam, N. Y., and the state normal school. In 1886 he graduated at the Bellevue Hospital Medical College, New York. Following his internship at the Presbyterian Hospital and Sloane Hospital for Women, New York, Dr. Madill joined the staff of the A. Barton Hepburn Hospital, Ogdensburg, serving there as chief surgeon since 1888.

Dr. Madill was a regent of the University of the State of New York, a fellow of the American College of Surgeons, a member of the New York Academy of Medicine, American Association for the Advancement of Science and the Alumni Association of New York University. In 1908 he received a doctor of laws degree from the St. Lawrence University, Canton, N. Y., and in 1932 one from New York University. He was president of the Medical Society of the State of New York in 1919, serving as trustee from 1926-1935. In 1925 he was president of the St. Lawrence County Medical Society. Dr. Madill had been first vice president of the St. Lawrence County Savings Bank and director of the Ogdensburg Trust Company. He was a member of the House of Delegates of the American Medical Association from 1912 to 1913, from 1922 to 1935 and from 1937 to 1940. He served as captain in the medical reserve corps of the U. S. Army, 1917-1918.



GRANT CHARLES MADILL, M.D.,
1864-1943

Clifton Meredith Miller ✠ Richmond, Va.; Medical College of Virginia, Richmond, 1892; associate professor of otolaryngology at his alma mater; specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology; member of the House of Delegates of the American Medical Association in 1912; member of the American Laryngological, Rhinological and Otological Society and the American Otological Society, Inc.; fellow of the American College of Surgeons; past president of the Richmond Eye, Ear, Nose and Throat Society, Virginia Ophthalmological and Otolaryngological Society and the Richmond Academy of Medicine; served as a member and vice chairman of the city school board of Richmond; local ophthalmologist, Seaboard Air Line Railway; member of the board of directors, ophthalmologist and otolaryngologist on the staff of the Stuart Circle Hospital; visiting surgeon, department of otolaryngology, Memorial Hospital; aged 69; died, February 26, of carcinoma of the prostate.

Thomas Joseph O'Leary ✠ Superior, Wis.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1906; past president of the State Medical Society of Wisconsin, the Douglas County Medical Society and the Interurban Academy of Medicine; councilor and past president of the Eleventh District of the State Medical Society; surgeon for the Great Northern and Soo Line railroads for many years; fellow of the American College of Surgeons; president of the Wisconsin State Bank and the Selective Service advisory board; chief of staff of St. Joseph's Hospital; on the staffs of St. Francis Hospital and St. Mary's Hospital, where he died, February 26, of coronary thrombosis, aged 61.

Ralph Rust Wilson ✠ Kansas City, Mo.; Harvard Medical School, Boston, 1921; specialist certified by the American Board of Obstetrics and Gynecology, Inc.; member of the Central Association of Obstetricians and Gynecologists; past president of the Kansas City Academy of Medicine and the Kansas City Obstetric and Gynecological Society; for many years chairman of the committee on maternal welfare of the Missouri State Medical Association; chief of the obstetric and gynecologic service at the Kansas City General Hospital; served on the staffs of the Menorah Hospital, Trinity Lutheran Hospital and St. Luke's Hospital, where he died, February 6, of coronary thrombosis, aged 46.

Clarke Sullivan, Dayton, Ohio; Chicago Homeopathic Medical College, 1904; member of the Ohio State Medical Association; first chairman and first president of the Dayton Obstetrical Society; during World War I served as a captain in the medical corps of the U. S. Army and as assistant chief of staff at Base Hospital, Camp Sherman, Chillicothe; served on the courtesy staff of St. Elizabeth and Good Samaritan hospitals; member of the board of trustees, member of the consulting staff and for many years chief of the obstetrical staff of the Miami Valley Hospital, where he died suddenly, February 13, of acute dilatation of the heart, aged 65.

Charles Walter Waddell ✠ Fairmont, W. Va.; Harvard Medical School, Boston, 1907; specialist certified by the American Board of Internal Medicine; in 1938 president of the West Virginia State Medical Association; member of the State Advisory Board, Department of Public Assistance and examiner for the State Compensation Commission; member of the medical advisory board number 3, West Virginia Selective Service; fellow of the American College of Physicians; director of the clinical laboratory and member of the staff of the Fairmont General Hospital; aged 65; died, March 29.

Elizabeth M. Baer, Roselle Park, N. J.; Hahnemann Medical College and Hospital, Chicago, 1898; aged 81; died, January 25, in the Belle Mead Sanatorium and Farm, Bellemead, of coronary sclerosis.

George Le Roy Brown, Chicago; Chicago Homeopathic Medical College, 1899; veteran of the Spanish-American War; aged 66; died, February 28, in the Passavant Memorial Hospital of cardiac failure and hypertension.

Julius J. Buel, Lakewood, Ohio; Universität Bern Medizinische Fakultät, Switzerland, 1885; a charter member of the staff of Lutheran Hospital, Cleveland, and for many years on the staff of St. John's Hospital, Cleveland; aged 82; died, January 18, of cerebral hemorrhage.

George Fletcher Bullard ✠ Elizabethtown, N. C.; North Carolina Medical College, Charlotte, 1915; aged 55; died, January 17, in the Veterans Administration Facility, Fayetteville, of carcinoma.

Herbert G. Cabbell, Lawrence, Kan.; Jenner Medical College, Chicago, 1912; member of the Kansas Medical Society; aged 55; died, January 13, of valvular heart disease.

Erasmus Taylor Camp, Gadsden, Ala.; Medical College of Alabama, Mobile, 1885; member of the Medical Association of the State of Alabama; past president of the Etowah County Medical Society; at one time county health officer; formerly a physician in charge of the Camp and Ralls' Hospital; aged 93; died, February 9, of prostatic obstruction and uremia.

Lawrence Cauffman, Masonville, N. J.; Medico-Chirurgical College of Philadelphia, 1890; aged 73; died, January 25, of cardiovascular renal disease.

Guy Chappell, Dawson, Ga.; Atlanta Medical College, 1897; member of the Medical Association of Georgia; chairman of the Selective Service Board, and county physician; past president of the Terrell County Medical Society; a captain in the medical corps of the U. S. Army during World War I; aged 67; died, January 15, of carcinoma of the prostate.

Morton Clofine ✠ Philadelphia; Long Island College of Medicine, Brooklyn, 1937; diplomate of the National Board of Medical Examiners; member of the Philadelphia Obstetrics Society; associate in gynecology at the University of Pennsylvania Graduate School of Medicine; on the staffs of the Mount Sinai, St. Agnes and the Graduate Hospital of the University of Pennsylvania, where he died, February 18, of abdominal lymphosarcoma with metastases, aged 29.

Solomon David Deren ✠ Syracuse, N. Y.; University of St. Vladimira Faculty of Medicine, Kiev, Russia, 1913; Syracuse University College of Medicine, 1924; served on the staff of the Syracuse State School; aged 61; died, January 5, of coronary occlusion, arteriosclerosis and hypertension.

John Vardeman Dillman, Louisville, Ill.; Missouri Medical College, St. Louis, 1899; member of the Illinois State Medical Society; served during World War I in the medical corps of the U. S. Army; for several years president of the Clay County State Bank of Louisville; aged 73; died, February 11, of cardiorenal disease.

John Otho Downey, New York; University of Pennsylvania Department of Medicine, Philadelphia, 1906; at one time a surgeon, lieutenant commander, U. S. Navy; served during World War I; aged 59; died, February 2, in St. Luke's Hospital of coronary thrombosis.

Howard Paul Durbin ✠ Kirkwood, Mo.; St. Louis University School of Medicine, 1927; aged 46; died, January 17, of coronary occlusion.

Thomas Burnham Enders ✠ Mystic, Conn.; College of Physicians and Surgeons, New York, 1891; aged 77; died, January 25, in the Lawrence and Memorial Associated Hospitals, New London, of chronic nephritis, arteriosclerosis and duodenal ulcer.

Charles Schuyler Harper, Berryville, Ark.; Barnes Medical College, St. Louis, 1909; also a pharmacist; received the doctor of public health degree from Tulane University, New Orleans, in 1916; aged 64; died, February 16, of heart disease.

Allen Fitch Higgins, Tampa, Fla.; Northwestern University Medical School, Chicago, 1902; physician of Hillsborough County for many years; served in the medical corps of the U. S. Navy during World War I; aged 67; died, February 3, in the Veterans Administration Facility, Bay Pines, of cerebral hemorrhage and arteriosclerosis.

Andrew Jackson Irwin, Sandersville, Ga.; University of Georgia Medical Department, Augusta, 1884; aged 80; died, January 25, of heart disease.

Homer Bates Jester ✠ Corsicana, Texas; College of Physicians and Surgeons, Baltimore, 1901; president of the Navarro County Medical Society; past president of the Central Texas District Medical Society; served as a major in the medical corps of the U. S. Army during World War I; for many years a member of the Navarro Clinic; a member of the board of directors of the State National Bank; aged 67; died, January 26, of coronary occlusion.

Rolfe Kingsley, New York; Columbia University College of Physicians and Surgeons, New York, 1906; associate in urology at his alma mater from 1924 to 1926; served as a genitourinary surgeon on the staff of the Presbyterian Hospital; aged 61; died, February 4, of cerebral hemorrhage.

John August Kussman, Piqua, Ohio; Medical College of Ohio, Cincinnati, 1889; aged 76; died, January 16.

Fannie Lanham, Chicago; Chicago College of Medicine and Surgery, 1913; a founder, a member of the board of trustees and for many years on the staff of the Women's and Children's Hospital; aged 71; died, January 27, at the home of her niece in Peoria, Ill., of carcinoma.

Albert H. Lanzer ✠ Cleveland Heights, Ohio; University of Wooster Medical Department, Cleveland, 1905; aged 66; died, January 16, of carcinoma.

Charles Lester Large, Portland, Ore.; College of Physicians and Surgeons, Keokuk, Iowa, 1880; aged 87; died, January 15, of cerebral hemorrhage.

Otto W. Lewke, Chicago; Chicago Medical College, 1889; member of the Illinois State Medical Society; chief physician to the coroner of Cook County from 1902 to 1909; member of the board of directors of the Chicago Public Library and vice president from 1897 to 1901; on the staff of the Norwegian-American Hospital; aged 76; died, March 7, of coronary thrombosis.

Washington E. Linden, Cleveland; Western Reserve University Medical Department, Cleveland, 1883; formerly member of the county board of health; aged 84; died, January 8, of lobar pneumonia.

John Othello Logan ✠ New York; Columbia University College of Physicians and Surgeons, New York, 1898; served on the staff of the Lutheran Hospital; aged 68; died, January 30, of cardiac decompensation.

Thomas F. Miller ✠ Lamar, Mo.; Missouri Medical College, St. Louis, 1899; past president and secretary of the Barton County Medical Society; served on the staffs of St. Luke's and General hospitals, Kansas City; aged 64; died, January 10, of coronary occlusion.

Joseph David Mitchell, Fort Smith, Ark.; College of Physicians and Surgeons, Little Rock, 1909; for many years associated with the Great Lakes Agency of the Indian Service at Lac du Flambeau, Wis.; aged 61; died, February 2, in the Veterans Administration Facility, Fayetteville, of nephritis.

Willard Elizabeth Park, Dallas, Texas; Rush Medical College, Chicago, 1909; aged 70; died, February 1, in a local hospital of burns received in a fire which destroyed an apartment house in which she was visiting.

J. Lampton Price, Frankfort, Ky.; Bellevue Hospital Medical College, New York, 1877; formerly health officer; aged 87; died, January 29, of arteriosclerosis.

George I. Reeves, Farnam, Neb.; Ensworth Medical College, St. Joseph, Mo., 1902; aged 82; died, January 23, in Burlington, Iowa, of hypostatic pneumonia.

George W. Ringgold, Gould, Ark.; Arkansas Industrial University Medical Department, Little Rock, 1886; member of the Arkansas Medical Society; aged 77; died, January 25, of coronary occlusion.

Edgar Allison Sears, Decatur, Neb.; Drake University Medical Department, Des Moines, Iowa, 1888; member of the Nebraska State Medical Association; for two years county superintendent of schools; associated with the Indian Service for many years; aged 83; died, January 29, of heart disease.

Solomon Thomas Shelly, Mulvane, Kan.; Missouri Medical College, St. Louis, 1883; member of the Kansas Medical Society; served on the staff of the Atchison, Topeka and Santa Fe Railway Hospital; aged 86; died, January 17, of hypostatic pneumonia.

William E. Waldrop, Parma, Idaho; Louisville (Ky.) Medical College, 1903; member of the Idaho State Medical Association; at one time county physician; veteran of the Spanish-American War; for many years a member of the board of trustees of the school board; formerly superintendent of the Idaho State Soldiers Home Hospital, Boise; aged 69; died, January 27, in Boise of pneumonia and heart disease.

Perry Trowbridge Walters, La Crosse, Wis.; University of Michigan Medical School, Ann Arbor, 1933; member of the State Medical Society of Wisconsin; secretary-treasurer of the La Crosse County Medical Society; on the staffs of the La Crosse Lutheran Hospital and the Gundersen Clinic; medical examiner for draft board number 1; aged 38; died, January 8, of carcinoma of the stomach with metastases.

Joseph M. Welch, Sutton, Neb.; Rush Medical College, Chicago, 1902; member of the Nebraska State Medical Association; served as mayor of Sutton and on the school board; on the staff of the Sutton Hospital; aged 64; died, January 26, of cardiorenal vascular disease.

Robert Minor Wiley, Salem, Va.; Medical College of Virginia, Richmond, 1895; member of the Medical Society of Virginia; aged 72; died, January 5, of paralysis agitans.

Philip L. Wise ✠ San Jose, Calif.; University of Southern California College of Medicine, Los Angeles, 1905; member of the Pacific Coast Oto-Ophthalmological Society; aged 62; died, January 8, of heart disease.

Katharine Woltmann, Delavan, Ill.; Hahnemann Medical College and Hospital, Chicago, 1904; aged 81; died, January 12, of cerebral hemorrhage.

William Purnell Yerger, Tallulah, La.; Memphis (Tenn.) Hospital Medical College, 1901; aged 65; died, January 8.

Stanley John Zolnowski ✠ Cleveland; St. Louis University School of Medicine, 1928; assistant in the department of pathology, 1925-1926 and teaching fellow in the same department, 1926-1927, at his alma mater; aged 40; died, January 6, of coronary thrombosis.

DIED WHILE IN MILITARY SERVICE

Claude Edwin Hale Jr., Marshall, Mich.; Vanderbilt University School of Medicine, Nashville, Tenn., 1917; member of the Michigan State Medical Society; served during World War I; captain in the medical corps, Army of the United States; aged 46; died, November 5, as the result of injuries received in a government vehicle in the Southwest Pacific area.

Eli Silberschein, Brooklyn; Regia Università degli Studi di Bologna. Facoltà di Medicina e Chirurgia, Italy, 1940; was an intern at the Israel Zion Hospital; first lieutenant in the medical corps of the Army of the United States called to active duty July 28, 1942; aged 26; was shot and killed at Yuma, Ariz., January 24.

Varnum Cochran Southworth, Cambridge, Md.; Detroit College of Medicine and Surgery, 1924; member of the Medical and Chirurgical Faculty of Maryland and the American Academy of Orthopaedic Surgeons; was called to active duty as a lieutenant commander, medical corps-V (S) U. S. Naval Reserve; aged 44; died, February 9, in Hartford, Conn., of heart disease as the result of pneumonitis.

Correspondence

HAZARD OF PARALDEHYDE ADMINISTRATION

To the Editor:—In THE JOURNAL, March 6, page 783, appears a communication by Dr. A. H. Miller in reference to my article on the "Hazard of Paraldehyde Administration," which appeared in the January 16 issue of THE JOURNAL.

I should like to repudiate all of Dr. Miller's criticisms:

1. Dr. Miller would propose a different caption for the paper, while he himself misquotes the original title.

2. Concerning the dosage for intravenous administration it is surprising to learn that an experienced anesthetist would employ a fixed, predetermined dose of 9 cc. as the maximum intravenous dose. Any anesthetic agent administered intravenously should be injected at the proper rate until the desired effect is attained. Granted that 9 cc. of paraldehyde intravenously is usually sufficient to produce anesthesia, there will be cases, as in the one described, in which this amount will be ineffective.

3. In his objection to the instillation by rectum of 35 cc. of paraldehyde as excessive, Dr. Miller failed to mention that it was administered three times at six hour intervals. The amount actually given was 15 cc. each time (a total of 45 cc. and not 35 cc., as again misquoted).

4. The most objectionable criticism is the casual statement that paraldehyde is "an agent which, if not the safest of hypnotics, is certainly as safe as any." To repudiate this statement would require reiteration of the entire original paper, in which is given some of the history relative to fatalities following paraldehyde administration, as well as to reiterate the experimental evidence as reported in that article.

CHARLES BURSTEIN, Captain, M. C., A. U. S.

TOXICITY OF HUMAN PLASMA

To the Editor:—Our attention has been drawn to some inaccuracies in your editorial on Toxicity of Human Plasma (THE JOURNAL, Sept. 19, 1942, p. 206).

In the first place you refer to the A and B group specific substances as haptens. There is now considerable evidence to show that they are antigens and not haptens. In the second place the statement that 50 per cent of group A and 85 per cent of group B serums contain the corresponding agglutinogen was qualified in our paper in the following way: "It should be mentioned here that the inhibition technic is not sufficiently sensitive to detect very small quantities of inhibiting substances" (*J. Path. & Bact.* **54**:92 [Jan.] 1942). "It is evident that amounts of agglutinogen too small to produce inhibition in vitro will yet produce a brisk response on injection. Although the inhibition test indicates that at least 50 per cent of group A and 85 per cent of group B persons have the corresponding agglutinogen in their serum and plasma, it seems likely that the true percentages are higher" (*ibid.*, p. 101). Thirdly, the terms serum agglutinogen and isoagglutinin have been confused; it was isoagglutinin and not agglutinogen titers which we estimated after pooling plasma from A and B donors. We made no estimation of residual agglutinogen after pooling; in view of the presence of free anti A and anti B isoagglutinins probably only small amounts of A and B agglutinogen were present.

E. F. AUBERT,
S.W. London Blood Supply Depot,
Benhill Avenue, Sutton, Surrey.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and Examining Boards in Specialties were published in THE JOURNAL, April 3, page 1170.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, June 15-16. Sec., Dr. B. F. Austin, 519 Dexter Ave., Montgomery.

ARKANSAS: * *Medical.* Little Rock, June 3-4. Sec., Dr. D. L. Owens, Harrison. *Eclectic.* Little Rock, June 3-4. Sec., Dr. C. H. Young, 1415 Main St., Little Rock.

CALIFORNIA: San Francisco, June 28-July 1. *Oral.* Los Angeles, August 9. Sec., Dr. Frederick N. Scatena, 1020 N Street, Sacramento.

DELAWARE: Dover, April 13-15. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: * Washington, May 10-11. Sec., Commission on Licensure, Dr. George C. Ruhland, 6150 E. Municipal Bldg., Washington.

FLORIDA: * Jacksonville, June 21-22. Sec., Dr. William M. Rowlette, Box 786, Tampa.

HAWAII: Honolulu, June 12-15. Sec., Dr. J. A. Morgan, 55 Young Building, Honolulu.

IDAHO: Boise, July 13. Director Bureau of Occupational Licenses, Mrs. Lela D. Painter, 355 State Capitol Building, Boise.

ILLINOIS: Chicago, June 22-24. Superintendent of Registration, Department of Registration and Education, Mr. Philip M. Harman, Springfield.

INDIANA, Indianapolis, Sept. 14-16. Sec., Board of Medical Registration & Examination, Dr. W. C. Moore, 301 State House, Indianapolis.

KANSAS: Kansas City, May 19-20. Sec., Board of Medical Registration and Examination, Dr. J. F. Hassig, 905 N. Seventh St., Kansas City.

LOUISIANA: New Orleans, May 6-8. Sec., Dr. R. B. Harrison, 1507 Hibernia Bank Bldg., New Orleans.

MARYLAND: *Homeopathic.* Baltimore, June 15-16. Sec., Dr. J. A. Evans, 612 W. 40th St., Baltimore.

MICHIGAN: * Ann Arbor and Detroit, June 11-13. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 100 W. Allegan St., Lansing.

NEVADA: Carson City, May 3. Sec., Dr. Richard A. Petty, 215 North Carson St., Carson City.

NEW JERSEY: Trenton, June 15-16. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: * Santa Fe, April 12-13. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NORTH CAROLINA: Raleigh, June 14-18. Sec., Dr. W. D. James, Hamlet.

NORTH DAKOTA: Grand Forks, July 6-9. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OKLAHOMA: * Oklahoma City, May 10. Sec., Dr. J. D. Osborn, Jr., Frederick.

OREGON: * Portland, April 21-24. Sec., Dr. L. S. Besson, 608 Failing Building, Portland.

SOUTH DAKOTA: * Pierre, July 20. Dir., Medical Licensure, State Board of Health, Dr. J. F. D. Cook, Pierre.

UTAH: Salt Lake City, June. Dir., Department of Registration, Mr. G. V. Billings, 324 State Capitol Bldg., Salt Lake City.

WYOMING: Cheyenne, June 7-8. Sec., Dr. M. C. Keith, Capitol Building, Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

CONNECTICUT: June 12. Sec., State Board of Healing Arts, Dr. C. M. Bakewell, 1945 Yale Station, New Haven.

DISTRICT OF COLUMBIA: Washington, April 19-20. Sec., Commission on Licensure, Dr. George C. Ruhland, 6150 E. Municipal Bldg., Washington.

FLORIDA: DeLand, June 9. Final date for filing application is May 24. Sec., Dr. J. F. Conn, John B. Stetson University, DeLand.

IOWA: Des Moines, April 13. Dir., Division of Licensure & Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

NEBRASKA: Omaha, May 4-5. Dir., Bureau of Examining Boards, Mrs. J. Crawford, 1009 State Capitol Building, Lincoln.

NEW MEXICO: June 14. Sec., Miss Pia Jœrger, State Capitol, Santa Fe.

OREGON: Corvallis, July 10. Sec., State Board of Higher Education, Mr. C. D. Byrne, University of Oregon, Eugene.

RHODE ISLAND: Providence, May 19. Chief, Division of Examiners, Mr. Thomas B. Casey, 366 State Office Building, Providence.

SOUTH DAKOTA: Aberdeen, June 4-5. Sec., Dr. G. M. Evans, Yankton.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Insanity: Criteria of Criminal Responsibility.—The defendant was convicted and sentenced to ten years' imprisonment for first degree robbery and appealed to the Supreme Court of Missouri. He admitted that the state's evidence was sufficient to support the conviction but on appeal contended that he was not capable of the intent required to be guilty of the offense in that he was mentally deficient and at certain periods, especially when he drank, he had not the capacity to distinguish right from wrong conduct.

There can be no doubt, said the Supreme Court of Missouri, but that legal mental capacity to commit a crime is an essential prerequisite to responsibility and a person cannot be legally punished for an act committed by him while insane, although the act would constitute a crime if done by a sane person. While the law recognizes the existence of many forms and degrees of insanity, mental incapacity excusing the commission of a crime must be such that the defendant is unable to distinguish right from wrong at the time of the commission of the offense, and the burden is on the defendant to prove the facts from which a jury may reasonably infer the fact of legal mental incapacity. Moronity, mere weakness of intellect, or subnormal mental capacity, is not in and of itself such insanity or mental incapacity as constitutes an excuse or defense to a crime. The total effect of the defendant's evidence in this case, the court pointed out, was not that he was insane but that he was a person of subnormal mental ability and capacity. This evidence does not prove insanity in the sense required by law. Broadly speaking, voluntary intoxication, regardless of the person's intellect, is not a defense to a criminal charge and has no bearing on it except in certain instances not involved in the present case. The defendant's argument, the court continued, was merely of the commonly known phenomenon that liquor does affect one, at least to the extent that he does not act and conduct himself as he normally does and would if he were not drinking. The defendant's experiences and reactions in this respect, however, presented nothing new or unusual, certainly not insanity or even delirium tremens induced by intoxication.

The defendant did not claim to have been intoxicated to the extent that the liquor totally deprived him of his reason or that he was insane but argued that, because he was a person of subnormal mentality and had been drinking, the combination of the two "laid a foundation" for the proof and defense of insanity of which he was deprived by the adverse ruling of the trial court on certain evidence offered. The trouble with this position, said the court, was that the only witness qualified to speak on the subject of the sanity of the defendant, a psychiatrist, stated that the defendant was sane when he examined him two years prior to the commission of the offense and that he had no opinion as to his mental condition after that time because he had not subsequently examined him. The evidence given by the lay witnesses to the effect that the defendant did not act or conduct himself as usual when he was drinking, that he kept his hands in his pockets and asked people for money when he was drinking were not such facts and circumstances from which they or any one else could draw the inference or express the opinion that he was insane or so lacking in mental capacity as to be excused from the charge of robbery if the jury believed him to be guilty under all the evidence.

The judgment of conviction was therefore affirmed.—*State v. Pinski, 163 S. W. (2d) 785 (Mo., 1942).*

Society Proceedings

COMING MEETINGS

Alabama, Medical Association of the State of, Birmingham, April 20-22. Dr. Douglas L. Cannon, 519 Dexter Ave., Montgomery, Secretary.

American Association of Industrial Physicians and Surgeons, Rochester, N. Y., May 25-27. Dr. E. C. Holmblad, 28 East Jackson Blvd., Chicago, Managing Director.

American Association on Mental Deficiency, New York, May 12-15. Dr. Neil A. Dayton, Mansfield Training School, Mansfield Depot, Conn.

American Gynecological Society, Hershey, Pa., May 31-June 2. Dr. Howard C. Taylor Jr., 842 Park Ave., New York, Secretary.

American Neurological Association, New York, May 6-7. Dr. Henry A. Riley, 117 East 72d St., New York, Secretary.

American Ophthalmological Society, Hot Springs, Va., May 31-June 2. Dr. Walter S. Atkinson 129 Clinton St., Watertown, N. Y., Secretary.

American Psychiatric Association, Detroit, May 10-13. Dr. Winfred Overholser, St. Elizabeth's Hospital, Washington, D. C., Secretary.

American Psychoanalytic Association, Detroit, May 9-11. Dr. Leo H. Bartemeier, General Motors Bldg., Detroit, Secretary.

American Society of Clinical Pathologists, Chicago, June 4-6. Dr. Alfred S. Giordano, 531 North Main St., South Bend, Ind., Secretary.

American Surgical Association, Cincinnati, May 13-14. Dr. Warfield M. Firor, Johns Hopkins Hospital, Baltimore, Secretary.

Arizona State Medical Association, Tucson, April 30-May 1. Dr. Frank J. Milloy, 112 North Central Avenue, Phoenix, Secretary.

Arkansas Medical Society, Little Rock, April 19-20. Dr. W. R. Brooksher, 602 Garrison Ave., Fort Smith, Secretary.

California Medical Association, Los Angeles, May 2-3. Dr. George H. Kress, 450 Sutter St., San Francisco, Secretary.

Connecticut State Medical Society, New Haven, May 25-27. Dr. Creighton Barker, 258 Church Street, New Haven, Secretary.

Florida Medical Association, Jacksonville, April 15-16. Dr. Shaler Richardson, 111 West Adams St., Jacksonville, Secretary.

Georgia, Medical Association of, Atlanta, May 11-14. Dr. Edgar D. Shanks, 478 Peachtree St. N.E., Atlanta, Secretary.

Illinois State Medical Society, Chicago, May 18-20. Dr. Harold M. Camp, 224 South Main St., Monmouth, Secretary.

Iowa State Medical Society, Des Moines, April 29-30. Dr. Robert L. Parker, 3510 Sixth Avenue, Des Moines, Secretary.

Maryland, Medical and Chirurgical Faculty of, Baltimore, April 27-28. Dr. W. Houston Toulson, 1211 Cathedral St., Baltimore, Secretary.

Massachusetts Medical Society, Boston, May 24-26. Dr. Michael A. Tighe, 8 Fenway, Boston, Secretary.

Minnesota State Medical Association, Minneapolis, May 17-19. Dr. B. B. Souster, 493 Lowry Medical Arts Bldg., St. Paul, Secretary.

Mississippi State Medical Association, Jackson, May 11-13. Dr. T. M. Dye, Clarksdale, Secretary.

Missouri State Medical Association, St. Louis, April 18-20. Mr. Raymond McIntyre, 634 North Grand Blvd., St. Louis, Executive Secretary.

National Tuberculosis Association, St. Louis, May 5-6. Dr. Charles J. Hatfield, 7th and Lombard Sts., Philadelphia, Secretary.

New Hampshire Medical Society, Manchester, May 11. Dr. Carleton R. Metcalf, 5 South State St., Concord, Secretary.

New Jersey, Medical Society of, Newark, May 25-26. Dr. Alfred Stahl, 55 Lincoln Park, Newark, Secretary.

New York, Medical Society of the State of, Buffalo, May 3-6. Dr. Peter Irving, 292 Madison Ave., New York, Secretary.

North Carolina, Medical Society of the State of, Raleigh, May 10-12. Dr. Roscoe D. McMillan, Red Springs, Secretary.

North Dakota State Medical Association, Bismarck, May 10-11. Dr. L. W. Larson, 221 Fifth Street, Bismarck, Secretary.

Northern Tri-State Medical Association, Ann Arbor, Mich., April 13. Dr. F. R. Nicholas Carter, 105 East Jefferson Blvd., South Bend, Ind., Secretary.

Oklahoma State Medical Association, Oklahoma City, May 11-12. Dr. Lewis J. Moorman, 210 Plaza Court Bldg., Oklahoma City, Secretary.

Rhode Island Medical Society, Providence, June 2-3. Dr. William P. Buffum, 122 Waterman St., Providence, Secretary.

Texas, State Medical Association of, Fort Worth, May 3-6. Dr. Holman Taylor, 1404 West El Paso St., Fort Worth, Secretary.

West Virginia Medical Association, Charleston, May 17-18. Mr. Charles Lively, 1031 Quarrier St., Charleston, Executive Secretary.

CENTRAL SOCIETY FOR CLINICAL RESEARCH

Fifteenth Annual Meeting, held in Chicago, Nov. 6 and 7, 1942

The President, DR. ARLIE R. BARNES, Mayo Clinic, Rochester, Minn., Presiding

(Continued from page 1176)

"Three to One" Modified Protamine Zinc Insulin

DRS. CYRIL M. MACBRYDE and HAROLD K. ROBERTS, St. Louis: The protamine zinc insulin now in use is not ideal for maintenance of control in many diabetic patients. The need for a type of insulin effective for at least twenty-four hours, but with sufficient rapid activity to prevent postprandial hyperglycemia, is widely recognized. In the past two and one-half years among 154 well controlled diabetic patients whom we have followed, 35 per cent required combined therapy with protamine zinc insulin and a separate morning injection of regular insulin. Nearly all patients needing over 40 units daily required combined therapy for good control. The most widely useful ratio consists of three parts of protamine zinc insulin to one of regular insulin. The combined method of treatment is objectionable, however, because it is a compromise, partly nullifying the advantages of the slow acting protamine zinc insulin. Two injections are still required, and the patient is obliged to manipulate two very different forms of insulin, multiplying the possibilities of error.

Comparative twenty-four hour blood sugar curves on 18 diabetic patients under controlled conditions showed great similarity between those obtained with protamine zinc insulin as compared with histone zinc insulin. Diabetic control was better with protamine zinc insulin, while histone zinc insulin failed to exhibit the desired more prompt action. Comparative curves with clear (acid, or soluble) protamine zinc insulin on 11 patients revealed better control with the market turbid protamine zinc insulin, while the clear insulin failed to give evidence of more rapid initial activity. Studies with globin insulin and other insulin modifications have been disappointing.

The most promising field proved to be mixtures of protamine zinc insulin and regular insulin. When protamine zinc insulin and regular insulin are mixed in the proportions employed when separately injected in the combined method of therapy, all or practically all of the insulin is precipitated. By combining equal parts of protamine zinc insulin and regular insulin, and adjusting the p_H to 7.2, however, it is possible to prepare a form of modified protamine zinc insulin which has the activity of three parts of protamine zinc insulin to one part of regular insulin, which is the proportion found most useful for the large majority of our patients. This special 3:1 modified protamine zinc insulin, when compared with protamine zinc insulin in 11 patients, gave better diabetic control with lower blood sugars during the day and equally good control of the night and fasting sugar levels. Comparison of 3:1 insulin with combined protamine zinc insulin and regular insulin therapy revealed somewhat better control with the 3:1 insulin than with the two separate injections. Six patients under controlled conditions showed comparatively little blood sugar fluctuations throughout the twenty-four hours, although in 4 cases the single dose administered was 70 units or over. Thus it would seem that a single injection of 3:1 modified protamine zinc insulin can take the place of market protamine zinc insulin in the regulation of mild diabetes when supplementary injections of regular insulin are not required and can also be substituted for the two separate injections required by most diabetic patients needing more than 40 units of insulin daily.

DISCUSSION

DR. R. M. WILDER, Rochester, Minn.: What criteria were used for adjusting the dosage day by day of the mixed insulin? Is the morning urine tested and a lower dose given when the morning urine is sugar free, or is some other time of testing better for determining whether the dose is satisfactory or not? We have also been giving mixed insulins for some time, not a fixed preparation such as Dr. MacBryde is using, but shifting the preparation, depending on the shifting daily requirements. Some people seem to do better with more protamine zinc insulin and less regular insulin; some, but not all, do well with preparations like those Dr. MacBryde has found satisfactory. The patient tests the urine twice daily, and we use the result of the morning test as the criterion of whether or not the protamine component is as high as we want it to be. The afternoon test tells whether the regular component should be increased or decreased. I would like to know, using fixed proportions, how Dr. MacBryde knows whether to increase or decrease the dose of the mixture. After he determines the dose in the hospital what criteria will the patient use at home?

DR. CYRIL M. MACBRYDE, St. Louis: Most of our studies have been done in the hospital on carefully controlled patients, with diets accurately weighed, all urines collected for quantitative sugar determinations, and blood sugars frequently determined. We have some patients now controlled with 3:1 insulin who are coming to the clinic or are seen as office patients. Our criteria for control are the same as those we have used in treating patients with protamine zinc insulin alone or with the combined treatment, using separate injections, each morning, of protamine zinc insulin and regular insulin. If the fasting blood sugar is too low and there is no glycosuria during the night or if there are any indications of hypoglycemia during the night or in the early morning, the patient may be getting too much protamine zinc insulin effect. If the blood sugar is too high at night or glycosuria occurs, we know that the protamine zinc insulin effect is not sufficient. On the other hand, the blood sugar two hours after breakfast and the glycosuria during the morning tell us whether we are getting enough of the rapid insulin effect. With 3:1 insulin we are encouraged by the fact that the controls in these two periods tend to go together. We are obtaining relatively flat curves throughout the twenty-four hours. Previously the night period reflected chiefly the effect of protamine zinc insulin, while the period after breakfast showed the response to the separate injections of regular insulin. With the new 3:1 modified protamine zinc insulin, giving 75 per cent prolonged effect and 25 per cent rapid effect, we have accomplished in most of our cases much better control throughout the twenty-four hours. I am much opposed to the use of extemporaneous mixtures of protamine zinc insulin and regular insulin. In the first place the rapid insulin effect is not obtained to any perceptible degree unless an amount of regular insulin at least equal to the amount of protamine zinc insulin is used. If the p_H is not readjusted to 7.2, the material injected is more acid than the tissue fluid and this introduces further variation in the rate of absorption. The great majority of patients should not and cannot be trusted to mix various forms of insulin for themselves. Most physicians are much too busy to worry with all the intricate details of numerous variable mixtures. The treatment of diabetes is complicated enough without making it more so. If the 3:1 insulin we have described can be substituted for the two separate injections previously needed for a large percentage of diabetic patients, it will simplify the problems both of patient and of physician.

Mechanism of the Action of X-Ray Therapy on Infection

DRS. J. DEWEY BISGARD and HOWARD B. HUNT, Omaha: In a series of rabbits the peritoneal cavity was inoculated with a culture of hemolytic colon bacillus establishing a constant minimal lethal dose. Two slants of a forty-eight hour culture invariably caused death of the animals within eight hours after inoculation. Sulfanilamide and sulfathiazole given in large therapeutic doses either by stomach, intravenously, subcutaneously or by implantation into the peritoneal cavity preceding or at the time of inoculation had no influence on the result of the inoculation. However, in a group of animals receiving 100 roentgens over the abdomen at periods varying from twenty-four to ninety-six hours before inoculation there were approximately 50 per cent survivals. Sixty per cent of the animals irradiated forty-eight hours before inoculation survived. From this survival peak there was a rapid decline so that there were

no survivals in those inoculated ninety-six hours after irradiation. All control animals inoculated at the same time died.

Because this culture produced such a rapidly fatal result it was decided to determine the effect of inoculating the peritoneal cavity with the killed culture. It was found that the killed culture was equally fatal and that preinoculation x-ray irradiation gave the same results as previously enumerated. It appeared therefore that the animals were not dying from a fatal infection but rather from a fatal toxemia and that irradiation caused the tissues to produce some factor capable of neutralizing the toxins.

In a third series blood was drawn from animals forty-eight hours after irradiation and the serum mixed with live cultures in one group and with killed cultures in another and these respectively were injected into the peritoneal cavities of stock rabbits. From 50 to 60 per cent of animals so treated survived. Thus it appears that the neutralizing effect of irradiation is not a local one but is the result of an antitoxic substance liberated into the blood stream. Irradiation gave about the same degree of protection to animals inoculated with a lethal dose of diphtheria toxin.

From these studies and from related ones which are still in progress it is our belief that the insult of irradiation to tissues causes them to liberate nonspecific antitoxic substances and that these substances are present in the blood stream and peritoneal fluid.

Comparative Study of Pathogenesis and Pathology of Pneumonitis in Infancy

DR. JOHN M. ADAMS, Minneapolis: The pathogenesis and pathology of nine different forms of pneumonia in infancy have been considered separately and comparatively, and only the distinctive pathologic-anatomic features have been related to the etiology and development of each entity. Three cases of sudden death due to pneumonitis have been presented. The study was conducted according to this outline:

1. Aspiration pneumonia (lipoid pneumonia).
2. Tuberculosis (first infection type of pneumonia).
3. Eosinophilic pneumonia (Loeffler's syndrome).
4. Interstitial pneumonia (whooping cough, measles and so on).
5. Primary virus pneumonitis.
6. Secondary virus pneumonia (Goodpasture).
7. Primary pyogenic pneumonia.
8. Secondary pyogenic pneumonia.
9. Syphilitic pneumonia (pneumonia alba).

Fat laden macrophages and foreign body giant cells set apart the pneumonias resulting from aspiration. In tuberculosis the epithelioid cell and enlarged mediastinal nodes characterize the entity. Widespread pulmonary infiltraton of the eosinophilic cell, coinciding with the high blood eosinophilia, is assumed for Loeffler's pneumonia, since there has been no opportunity to study autopsy specimens. The blood eosinophils are larger than normal, with unusually large granules, which are fewer in number.

The thickening of the various constituents of the pulmonary system seen in interstitial pneumonia is distinctive. The peribronchiolitis with small round cell infiltration adds to the picture. The features of primary virus pneumonitis are similar, with ulceration and proliferation of epithelial lining membranes plus the presence of cytoplasmic inclusion bodies in the epithelial cells. The secondary form has intranuclear inclusions in the epithelial structures as its specific differentiating feature.

The presence of leukocytes and specific bacteria with abscess formation and empyema distinguish the pyogenic pneumonias. Syphilitic pneumonia is characterized pathologically by the extreme hyperplasia of the fibrous elements and the presence of Treponema pallidum.

From an immunologic point of view the immature lung of infancy is a most vulnerable organ, being readily susceptible to nearly all forms of pneumonia. Primary agents such as the pyogenic bacteria and pneumotropic viruses may produce fulminating disease and even sudden death.

DISCUSSION

DR. W. E. BROWN, Omaha: A few months ago inclusion body blennorrhea developed in a child who had been delivered by elective cesarean section; the amniotic membranes had not been ruptured. There was some curiosity as to this infection at birth in a child with no lung defect. The mother was apparently normal. An investigation was then begun of the vaginal epithelium of apparently normal women. To our surprise, various forms of inclusion body intracellular and extracellular organisms were present in 22 out of 25 normal women. We have raised the question at the University of Nebraska whether these inclusion bodies have anything to do with virus or are large toxic granules. In children we find these inclusion bodies in osteomyelitis and other infections in which virus is not usually encountered.

DR. JOHN M. ADAMS, Minneapolis: In our babies in two epidemics we have had no conjunctivitis. Inclusion blennorrhea begins from the fifth to the tenth day of life. The average age at onset of pneumonitis was 7 + weeks. We have observed this disease in babies as old as 6 or 7 months, particularly prematurely born babies after they have passed the period of immaturity; they still are apparently more susceptible to this disease. I cannot say how significant the finding of inclusions is in the sputum. We are at present studying the sputum of a good many patients with other diseases. We have not observed primary virus pneumonitis outside of small infants. Broadhurst in New York has found inclusion bodies in the sputum of adults, nurses and doctors suffering from upper respiratory infection.

Treatment of Acute Bacillary Dysentery (Flexner) with Sulfaguanidine and Succinylsulfathiazole

DRS. CHARLEY J. SMYTH, SYLVESTER E. GOULD and MORRIS B. FINKELSTEIN, Eloise, Mich.: During an outbreak of acute diarrhea 86 patients were studied. From the stools of 25, Shigella paradysenteriae (variety Flexner) organisms were cultured. Thirteen patients were treated with sulfaguanidine and, of these, 9 had positive stool cultures; 25 patients were treated with succinylsulfathiazole and 14 of these had positive stool cultures. With few exceptions, the dosage of sulfaguanidine was 0.1 Gm. per kilogram of body weight initially, and a maintenance dose of one half of this was given every four hours. The dosage of succinylsulfathiazole was 0.25 Gm. per kilogram of body weight initially and 0.25 Gm. per kilogram daily divided into six equal portions given every four hours.

The results of this study indicate that the new sulfonamide compound succinylsulfathiazole has no definite advantage over sulfaguanidine in its effect on fever, diarrhea and time required for stool cultures to become consistently negative. Although both drugs were administered in the doses recommended by other investigators, a recurrence of positive stool cultures was observed once after each drug. Five fatalities occurred; three were of untreated patients; 1 was treated with sulfaguanidine and the other with succinylsulfathiazole.

Determinations of the blood concentrations revealed that sulfaguanidine was absorbed to a greater extent than succinylsulfathiazole. A concentration of 16.6 mg. of sulfaguanidine per hundred cubic centimeters following the administration of 27 Gm. of this drug in three days was observed in 1 case. In no instance did the blood concentration of free sulfathiazole exceed 1.39 mg. per hundred cubic centimeters or the total succinylsulfathiazole 1.45 mg. per hundred cubic centimeters. No significant changes were observed in hemoglobin and white blood cell counts following the use of either drug.

The effect of the administration of a second course of these drugs on twenty patients was investigated; 11 received sulfaguanidine and nine succinylsulfathiazole. Three of the patients given the second course of sulfaguanidine manifested definite signs of toxicity, but no reactions followed the readministration of succinylsulfathiazole.

We believe that the two drugs are equally effective in the treatment of these cases, but because succinylsulfathiazole is potentially less toxic it is the drug of choice. Repeated stool cultures to detect carrier states following sulfonamide therapy of acute bacillary dysentery (Flexner) are necessary.

DISCUSSION

DR. G. F. KEMPF, Indianapolis: I should like to know what advantage either of these drugs has over sulfathiazole in this disease.

DR. M. A. BLANKENHORN, Cincinnati: I think it is extremely difficult to demonstrate the value of a drug in a disease as variable as dysentery and, moreover, to compare two drugs and say which is better. I would understand this epidemic better if Dr. Smyth would say something of the circumstances of the outbreak, particularly the day of the disease on which the patient was put on treatment. He was fortunate to have the epidemic in his institution, where he could get a good idea of its intensity, rather than in a general hospital, where only an occasional case is seen. I have seen a rather generous sprinkling of cases and I am undecided about the value of either of these drugs in dysentery. I think the mortality rates cited are rather high. I think 2, 3 or 4 per cent is a fair estimate of the mortality rate. Will he tell us more of the circumstances of the epidemic and state the day of the disease in which treatment was started?

DR. H. MARVIN POLLARD, Ann Arbor, Mich.: I should like to ask Dr. Smyth if he found any organism other than Flexner's dysentery bacillus in the stool cultured, and if so whether succinylsulfathiazole had any effect on them. During the past several months I have treated 12 cases of chronic ulcerative colitis with succinylsulfathiazole. Four of these patients had a prompt drop in temperature and the others had a gradual fall of temperature. In general the stools became less frequent, and blood disappeared from the stools completely in a period of one to three weeks. One patient has received up to 1,200 Gm. and none of these patients have had any type of reaction that could be directly attributed to the drug. In general, I feel that it is a safe and valuable adjunct to the other forms of treatment necessary for these individuals.

DR. CHARLEY J. SMYTH, Eloise, Mich.: We have had no experience with sulfathiazole in the treatment of dysentery. Yannet and his associates in Connecticut reported more rapid clinical recoveries in cases with Sonne dysentery treated with sulfathiazole but pointed out that there was a significant prolongation of the time required before the rectal cultures became consistently negative as compared with a control group. From our study of these relatively few cases we feel that, if succinylsulfathiazole is given in the amounts we have indicated, positive stool cultures can be controlled effectively and the course of the disease, as judged by fever and diarrhea, shortened. The epidemic that we studied occurred in two wards of a mental and general hospital with a total population of 9,000. All patients suspected of having dysentery were segregated at once in an isolation ward. There were many chronically ill and debilitated patients, and perhaps the high death rate may be due to that fact. No other pathogenic organisms of any significance were recovered. Although the final decision regarding the value of succinylsulfathiazole will be based on further clinical use, the results of this comparative study indicate that it provides a definite advance in the treatment of this important enteric disease.

The Effect of Arsenic (Solution of Potassium Arsenite) on Erythropoiesis

DR. LOUIS R. LIMARZI, Chicago: Following the oral administration of arsenic in relapsing cases of pernicious anemia the bone marrow shows severe toxic and destructive changes in the megaloblastic tissue consisting of various phases of caryorrhexis. A reticulocytosis as high as 18 per cent is observed peripherally in some cases without improvement in the anemia. The icteric index is not increased. If liver extract is administered to such a patient there is a normoblastic stimulation with an improvement in the anemia. The caryorrhetic fragments of the megaloblasts can still be observed for four or five days.

The oral administration of arsenic to normal controls and to persons with sickle cell anemia, erythroblastosis, hypochromic anemia, cirrhosis of the liver, carcinoma of the stomach and polycythemia vera in which the bone marrow consists of moderate to severe erythroid hyperplasia and immaturity produces no significant degenerative changes in the normoblasts. In spherocytic jaundice and in 1 case of refractory anemia with macrocytosis following the administration of arsenic, caryorrhexis in the polychromatic and orthochromatic normoblasts in the bone marrow is a conspicuous feature.

In none of the bone marrows is the pronormoblast affected by arsenic.

It is concluded that (1) the megaloblast in the bone marrow of relapsing cases of pernicious anemia is arsenic sensitive and the pronormoblast seen in normal marrow and in the bone marrow of most cases of anemia with an erythroid immaturity is arsenic resistant, (2) the "liver principle" can exert its physiologic effect on the bone marrow in pernicious anemia in the presence of a caryorrhetic megaloblastic tissue which presumably is in a poorly functional condition due to the toxic effect of arsenic and (3) the action of the hemopoietic principle is probably to effect the elimination (maturation) and suppression of the megaloblasts in the bone marrow. It is still not clear as to how the liver extract effects a stimulation of the normoblastic tissue. It is clear that arsenic has no such effect.

Effect of Breathing 80 to 100 Per Cent Oxygen on the Erythrocyte Equilibrium in Patients with Sickle Cell Anemia

DR. EDWARD H. REINHARD, DR. CARL V. MOORE, R. DUBACH, PH.D., and DR. LEO J. WADE, St. Louis: The effect of prolonged administration of 80 to 100 per cent oxygen to patients with sickle cell anemia has been observed. The study was undertaken to determine whether the oxygen tension of arterial blood could be raised sufficiently to decrease the intravascular sickling of red cells. It was thought that this might accomplish (1) a reduction in the rate of hemolysis with consequent lessening of the degree of anemia and (2) relief of pain during sickle cell crises. Observations have been made on 3 patients at six different times. After control periods of four to eight days the subjects were fitted with a Boothby-Lovelace-Bulbulian mask and given pure oxygen without intermission for eight to twenty days. Red cell counts, hemoglobin levels and reticulocytes were estimated daily. Determinations of serum iron and of oxygen content and capacity of both arterial and venous blood were made every four days. Excretion of urobilin in urine and stool was measured as an index of the rate of hemoglobin destruction (method of C. J. Watson). The percentage of sickled cells in arterial and venous blood was determined regularly (I. J. Sherman's method). Alveolar oxygen content was measured on several occasions.

Administration of nearly 100 per cent oxygen to these patients when they were having abdominal or muscular pain did not regularly give them relief. However, within a short time after the flow of oxygen was started the percentage of sickled cells in both venous and arterial blood decreased definitely, often from over 40 per cent to less than 20 per cent in the venous circulation. This change persisted as long as pure oxygen was breathed. The oxygen content of the arterial blood was increased so that it equaled or exceeded the oxygen capacity. No consistent change occurred in urobilin excretion, however, to indicate that the rate of hemolysis had been materially altered. The most dramatic results of prolonged oxygen administration were (1) a fall in reticulocytes, which usually began on the fourth to sixth days and which lowered the level from the initial 20 to 30 per cent to as low as 1 per cent, and (2) a fall in the erythrocyte count, which usually began on the sixth to eighth days and was as great as 0.5 to 1.5 million cells. After oxygen was discontinued, the reticulocytes began to increase and reached a peak of occasionally more than 50 per cent on the fifth to eighth days. A shower of normoblasts appeared concomitant with the reticulocytosis. At the same time the red cell levels began to increase and the rise continued until the preoxygen level had been attained. These results are interpreted as indicating that the administration of nearly 100 per cent oxygen depresses erythropoiesis, an effect which might be the physiologic antithesis of the erythroid stimulation produced by low oxygen tensions. It is suggested that this result has not been noted in previous studies when high concentrations of

oxygen were given to normal persons and to individuals with polycythemia because the length of red cell life is so great that the decreased rate of erythrocytogenesis would not be evident for long periods. Patients with sickle cell anemia show the effect more quickly because their reticulocyte level is elevated and their rate of red cell destruction accelerated.

No distinct toxic manifestations of the oxygen administration were noted except for inflammation and congestion of the mucous membranes of the upper respiratory passages. After oxygen was discontinued, 2 of the 3 patients became nauseated and had headaches for twenty-four to forty-eight hours.

DISCUSSION

DR. C. J. WATSON, Minneapolis: The alteration of the reticulocytes following the administration of oxygen is interesting. I think that the hypothesis offered is the only one that is tenable. It would be interesting to see what would happen to the reticulocyte count in hemolytic jaundice if oxygen should be given. I was most interested in the effect of oxygen and the way these patients tolerate oxygen. From the work Payne did with dogs I would not have expected patients to tolerate oxygen for so long. Payne found that in the dog several hours of 100 per cent oxygen often caused severe changes and after twenty-four hours death with contraction of the spleen commonly ensued. As the percentage of oxygen decreased the animals tolerated it better; 80 per cent oxygen could be tolerated for a long period without untoward effect.

DR. EDWARD H. REINHARD, St. Louis: We have not studied the effect of high oxygen tensions on the blood of patients with hemolytic anemia. We did wonder if the inhalation of oxygen by patients with pernicious anemia might prevent the usual reticulocyte response to liver therapy. This was tried on 1 such patient with equivocal results. We are planning to repeat these investigations on patients with various types of anemia. As to the toleration of oxygen by our patients, we have no completely satisfactory explanation as to why they developed no serious toxic manifestations. Our patients wore oronasal masks at night and nasal masks during the day. It has been shown that, when a person wearing a nasal mask talks or eats, the oxygen concentration of the inspired air decreases definitely. Undoubtedly this was a factor in preventing the development of oxygen intoxication.

The Response to Heparin: A Test of the Clotting Mechanism

DRS. GEZA DE TAKATS and N. C. GILBERT, Chicago: Following the intravenous injection of a 10 mg. dose of heparin, coagulation times have been determined at ten minute intervals. One hundred and fifty-four tests were made on 67 patients. A normal response was plotted from an average of fifty curves. A group of hyporeactors were found who showed varying amounts of resistance to heparin. They were patients in the early postoperative period, patients examined within a few days after an intravascular thrombosis and patients suffering from Buerger's disease. It was found that both digitalis and epinephrine have a depressing effect on heparin response. Conversely, a group of hyperreactors were encountered who showed clinical signs and symptoms of sensitization together with an exaggerated response to heparin. They may or may not have received heparin previously.

Compounds containing sulfur seemed to augment the action of heparin. The action of heparin on the coagulation time is biphasic and the relationship of the curves to one another indicates that any drug which exaggerates the first curve will tend to depress the second.

Based on these observations, it is suggested that no patient be heparinized unless a heparin curve is previously determined. The best and simplest method of administration is the intermittent injection of 50 mg. of heparin every three to four hours, with an adequate check on coagulation times. The length of administration need not exceed three days, after which dicumarol can be started. While heparin is more expensive and needs intravenous injections, its dosage is easily controlled, whereas dicumarol is given orally but requires daily prothrombin levels, which are unobtainable except in large hospitals.

DISCUSSION

DR. L. N. KATZ, Chicago: May I ask if observations on the heparin reaction in patients with Buerger's disease have been made to see whether the decreased sensitivity preceded or followed its onset?

DR. OVID O. MEYER, Madison, Wis.: Some people are hyposensitive to dicumarol and some are hypersensitive, but the hyporeactors are more numerous. I am not certain of the method employed in determining the coagulation time in this series. I presume, because of the short coagulation times reported, that it was done by the capillary method. The coagulation time of the so-called hyposensitive individuals was less than a minute shorter than that of the normal reactors. This difference would scarcely seem to be significant. If the capillary coagulation time is used, one must admit that it is relatively crude. I favor the determination of the coagulation time on venous blood. Although there are plenty of fallacies in the method of Lee and White, it appears that they are less numerous than when capillary blood is used. The importance of determining the coagulation time frequently when using heparin is well recognized. It is my practice, for at least the first day of heparin administration, to determine the coagulation time every few hours. It is now the usual practice for a patient who has thrombosis already developed to administer heparin intravenously for the prompt effect because with dicumarol there is a latent period of about twenty-four hours, and this is true whether the preparation is administered intravenously or orally. At the time of the heparin administration we begin oral administration of dicumarol. We can tell when the latter substance becomes active because the prothrombin time, which is unaffected by heparin, will be prolonged. Then the heparin is omitted and dicumarol therapy alone is continued.

DR. ARMAND QUICK, Milwaukee: This paper brings out the fact that heparin itself is not an anticoagulant but becomes so only when it reacts with something in the blood which presumably is albumin but which is probably best called albumin X. It is this albumin X which forms the true anticoagulant with heparin. It appears probable that the serum factor may vary, which accounts for the hypoactivity and hyperactivity of heparin in various bloods. I agree with Dr. Myers' remarks on the coagulation time. A committee should be formed to standardize the determination of the coagulation time. The coagulation time determined according to the procedure of Lee and White yields much more satisfactory and uniform results if the temperature is kept constant (37 C.). It has been observed that hemophilic blood which clots in two or three hours at 37 C. may at room temperature require twenty-four hours for clotting.

DR. FRANK H. BETHELL, Ann Arbor, Mich.: I should like to ask Dr. de Takats if he has studied the prothrombin time in relation to reactions.

DR. GEZA DE TAKATS, Chicago: If one produces a thrombosis in the lower extremity with a sclerosing solution there is usually a flattening of the heparin curve. A patient with deep femoral thrombosis presents a flattening of the heparin curve which disappears after ligation of the vein. It is quite probable that the flat curves are the result of the clot. On the other hand, it is also true that one can pick up patients with a flat postoperative curve, and this is particularly observed in the gynecologic service. We feel that, if the patient has a flat heparin curve after the fourth postoperative day, thrombosis is likely. We had 5 such patients, 1 of whom developed embolism and 4 postoperative thrombosis. We now use dicumarol after two days of heparin. The action of the latter drug is prolonged. We are perfectly aware that Lee and White's method is the standard method for blood coagulation. We still believe, however, that the capillary coagulation time is useful. We were anxious to devise a method that could be run by nurses or interns in any hospital. We get errors with the capillary method, but the percentage of error is the same during the test. Dr. Quick mentioned that heparin itself is not an anticoagulant, that it is only an activator. Heparin does not seem to do anything to the prothrombin time. Our difficulty with the administration of dicumarol is that unless the prothrombin time is determined by skilled technicians dicumarol is dangerous. One dislikes to use dicumarol because of the difficulty of adequate control.

(To be continued)

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1932 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Psychiatry, New York

99:317-474 (Nov.) 1942. **Partial Index**

Musician's Point of View Toward Emotional Expression. H. Hanson, Rochester, N. Y.—p. 317.

Irresponsibility of Juvenile Delinquents. D. A. Thom, Boston.—p. 330.

Course in Military Neuropsychiatry. R. D. Halloran and P. I. Yakovlev, Waltham, Mass.—p. 338.

Social Data in Psychiatric Casualties in the Armed Services. A. Simon and Margaret Hagan, Washington, D. C.—p. 348.

Aircrew Selection. H. D. Mitchell, Trenton, Ont., Canada.—p. 354.

Wartime Tasks of Psychiatric Social Workers in Great Britain. Mildred C. Scoville, New York.—p. 358.

Nonconvulsive Electric (Faradic) Shock Therapy of Psychoses Associated with Alcoholism, Drug Intoxication and Syphilis: Psychosomatic Approach in Treatment of "Reaction in Delirium." N. J. Berkwitz, Minneapolis.—p. 364.

Spinal Injuries in Shock and Epileptic Convulsions. J. E. Barrett, J. B. Funkhouser, Marion, Va., and W. A. Barker, Roanoke, Va.—p. 387.

Treatment of Psychoses with Long Protracted Insulin Coma. J. Wortis, M. Terris and I. M. Korr, New York.—p. 391.

Evaluation of Effects of Intravenous Insulin Technic in Treatment of Mental Diseases: Follow-Up Study of Group of Patients Treated with Intravenous Injection of Unmodified Insulin and Zinc Insulin Crystals. P. Polatin and H. Spotnitz, New York.—p. 394.

Investigation of Effect of Inhalation of 9 per Cent Oxygen for Twenty Minutes in Nonpsychotic and Schizophrenic Male Subjects. W. L. Holt Jr., Worcester, Mass.—p. 406.

Prefrontal Lobotomy in Chronic Psychoses. M. C. Petersen, Willmar, Minn., and H. F. Buchstein, Minneapolis.—p. 426.

Role of Psychiatric Social Worker in Selection of Men for the Armed Forces. Marian McBee and G. S. Stevenson, New York.—p. 431.

What Unemployment Does to People: Study in Adjustment to Crisis. S. W. Ginsburg, New York.—p. 439.

American Journal of Surgery, New York

59:1-158 (Jan.) 1943. **Partial Index**

Abdominal Cardiectomy or Subtotal Gastric Resection for Cancer of Proximal Half of Stomach: Case Report. G. T. Pack and C. S. Cameron, New York.—p. 3.

Pilonidal Cyst: Report of New Procedure for Operation and Treatment. D. Brezin, Fort Bragg, N. C.—p. 18.

Comminuted Fractures and Fracture Dislocations of Body of Astragalus: Operative Treatment. H. C. Blair, Portland, Ore.—p. 37.

Levator Ani, Coccygeus and Piriformis Muscles: Agents in Causation of Coccygodynia, Superior Gluteal Pain and Sciatic Syndrome. T. Wilensky, New York.—p. 44.

Cesarean Section: Evaluation of Types of Section and Their Indications. E. A. Schumann, Philadelphia.—p. 50.

Additional Experiences with Spool Cotton as Suture Material. P. Thorek, R. Gradman and A. Glaess, Chicago.—p. 68.

*New Type of Relaxing Incision—Dermatome Flap Method. H. N. Harkins, Detroit.—p. 79.

Control of Somatic Pain. W. Bates, Philadelphia.—p. 83.

Curative Treatment of Hemorrhoids. E. Granet, Guantanamo Bay, Cuba.—p. 87.

Differential Diagnosis Between Thymic Duct Fistulas and Branchial Cleft Fistulas: Report of Case of Bilateral Aural Fistulas and Bilateral Thymic Duct Fistulas. C. J. Baumgartner and S. Steindel, Los Angeles.—p. 99.

Human Red Cell Concentrate for Surgical Dressings. J. J. Moorhead and L. J. Unger, New York.—p. 104.

New Type of Relaxing Incision.—A new relaxing incision which combines the advantages of primary closure by a cutaneous graft and eliminates the necessity of making a separate wound to obtain closure is described by Harkins. It consists of a dermatome graft which is left attached at one end and reflected back. The incision is then made in the donor area or bed of the graft and the flap is turned down again to cover the raw area made by the incision. This method is especially applicable to wounds of the extremities from which large superficial tumors or scars are excised.

Annals of Surgery, Philadelphia

117:1-160 (Jan.) 1943

Cleft Palate. G. M. Dorrance and J. W. Bransfield, Philadelphia.—p. 1.

Mechanism of Shock in Intestinal Strangulation: Experimental Study. E. I. Evans, Boston.—p. 28.

Fluid, Protein and Electrolyte Alterations in Experimental Intestinal Obstruction. W. E. Abbott, R. C. Mellors and E. Muntwyler, Cleveland.—p. 39.

*Study of Plasma Protein Variations in Surgical Patients. D. Casten, M. Bodenheimer and I. Barcham, New York.—p. 52.

Carcinoma of Gum. G. S. Johnson and R. A. Daniel Jr., Nashville, Tenn.—p. 74.

Rate of Epithelial Regeneration: Clinical Method of Measurement and Effect of Various Agents Recommended in Treatment of Burns. B. Cannon and O. Cope, Boston.—p. 85.

*Intrathoracic Neuroblastoma: Case Report. W. E. Lee and J. A. Ritter, Philadelphia.—p. 93.

Empyema Complicated by Bronchoesophagopleural Fistula. J. K. Berman and C. E. Walters, Indianapolis.—p. 100.

Substitution of Urinary Bladder with Segment of Sigmoid: Experimental Study. J. D. Bisgard, Omaha.—p. 106.

So-Called Retroperitoneal Lipoma: Report of Seven Cases. J. S. Regan, S. Sanes and J. D. MacCallum, Buffalo.—p. 110.

Surgical Treatment of Congenital Malformations Implicating Distal Spinal Cord. J. Browder, Brooklyn.—p. 118.

Treatment of Congenital Hemangiomas of Skin. G. S. Johnson and R. A. Light, Nashville, Tenn.—p. 134.

Surgical Treatment of Intrinsic Knee Joint Lesions: Further Analysis of Operative Cases. J. J. Moorhead and D. Lyall, New York.—p. 140.

Light, Compact Unit for Intravenous or Intraosseous Injection of Plasma in Emergencies. Alison H. Price and L. M. Tocantins, Philadelphia.—p. 152.

Plasma Protein Variation in Surgical Patients.—In 215 consecutive surgical patients admitted to the Hospital for Joint Diseases, Casten and his collaborators tried to determine the incidence of hypoproteinemia associated with operations and its relationship to various procedures, the factors which influence changes in plasma proteins, the relationship between hepatic disorders and hypoproteinemia and ways of preventing and treating hypoproteinemia. Following the operative procedure, plasma proteins and hematocrit were determined immediately and thereafter every twelve to twenty-four hours until the patient recovered. A significant decline in the plasma protein level was observed in 148, or 68.9 per cent, of the patients. The decline was more common after operations on the stomach and intestine, the biliary tract, the spine and large joints and for toxic thyroid disorders. Among the many direct factors which influenced the extent and duration of the diminished protein concentration were blood loss, shock and anesthesia, while the indirect causes were the nutritional status of the patient, extent of the protein reserves and the adequacy of hepatic function. Depreciation because of blood loss and shock was usually of short duration and readily amenable to therapy, but when the protein reserves were exhausted or hepatic function was disturbed the depletion was prolonged and frequently response to treatment was irregular. As the hepatic function is known to be disturbed frequently in certain surgical conditions of an extrahepatic nature, the hepatic function of such patients should be tested routinely and the data should guide subsequent therapy. In the operations known to be almost constantly associated with much loss of protein the estimated loss should be replaced during operation by blood or plasma transfusions. If protein reserves are thought to be exhausted, the operation should be postponed until the reserves are restored by dietary therapy high in amino acids or the feeding of amino acids if the dietary cannot be given. Plasma is a readily available and potent source of protein and often proves efficacious when dietary therapy fails.

Intrathoracic Neuroblastoma.—Lee and Ritter report the case of a 5 month old infant who had puzzling symptoms and was finally diagnosed as having intrathoracic neuroblastoma as the result of aspiration biopsy under fluoroscopic guidance. Though the infant's condition was fair at the close of operation, he died about three and a half hours later. At necropsy the cavity on the right side of the chest contained about 75 cc. of dark red blood. The lung on the right side was fully collapsed and the one on the left was well aerated. The cause of death was probably hemothorax and associated shock. The diagnosis from a pathologic examination of the tumor was an atypical neurocytoma, there were hemorrhagic areas in the spleen, the lung on the right side was atelectatic and the one on the left

was normal, and the adrenals, kidneys and sternum were apparently normal. Early recognition of these tumors and prompt surgical and roentgen treatment will materially enhance the prognosis.

Archives of Neurology and Psychiatry, Chicago

49:1-150 (Jan.) 1943

Regenerative Capacity of Ventral Roots After Avulsion from Spinal Cord. Sarah S. Tower, Baltimore.—p. 1.
Studies in Diseases of Muscle: Progressive Muscular Atrophy: Report of Case with Unusual Features; Effect of Prostigmine and Physostigmine on Fasciculations; Metabolism of Ascorbic Acid. A. T. Milhorat and T. P. Almy, New York.—p. 13.
Fascicular Muscle Twitchings in Amyotrophic Lateral Sclerosis: Their Origin. R. L. Swank and J. C. Price, New York.—p. 22.
Familial Type of Paralysis in Infants and Its Relationship to Other Heredofamilial Disorders: Clinicopathologic Study. A. J. Lubin, San Francisco; O. Marburg, New York, and K. Tamaki, San Francisco. —p. 27.
Experimental Neuroses and Psychotherapy. J. H. Masserman, Chicago. —p. 43.
Constitutional Differences Between Deteriorated and Nondeteriorated Patients with Epilepsy: Capillaries of Finger Nail Fold. H. A. Paskind and M. Brown, Chicago.—p. 49.
Intracranial Dermoid and Epidermoid Tumors. J. Martin and L. Davis. —p. 56.
Sibling Deaths in Anamneses of Schizophrenic Patients. S. Rosenzweig and D. Bray, Worcester, Mass.—p. 71.
Distribution of Iodine in Blood Serum and in Cerebrospinal Fluid. E. F. Gildea and Evelyn B. Man, New Haven, Conn.—p. 93.
Functional Representation in Oculomotor and Trochlear Nuclei. M. B. Bender and E. A. Weinstein, New York.—p. 98.
Fatalities Following Electric Convulsive Therapy: Report of Two Cases, with Autopsy. F. G. Ebaugh, C. H. Barnacle and K. T. Neubuerger, Denver.—p. 107.
Acute Syphilitic Anterior Poliomyelopathic Syndrome: Report of Case. L. F. Barker, Baltimore.—p. 118.
*Arterial Hypertension Following Metrazol Shock Therapy. W. C. Menninger, Topeka, Kan.—p. 120.
Apparatus to Be Used in Recording Tremors. A. A. Morris Jr., Durham, N. C.—p. 123.

Hypertension After Metrazol Shock Therapy.—Menninger reports an instance in which hypertension has persisted for four years since metrazol shock treatment. The mechanism of the cardiovascular dynamics is not clear. The author believes that the anxiety and the fear connected with each treatment were as important in producing the hypertension as was the drug or the convulsions. The psychiatric picture did not change at the time, either as a result of therapy or with the onset of hypertension, but it did twelve months later after psychotherapy. The blood pressure has remained between 175 and 180 systolic and 115 and 125 diastolic as compared to the initial pressure, before metrazol shock therapy was begun four years ago, of 110 systolic and 80 diastolic.

Indiana State Medical Assn. Journal, Indianapolis

36:1-54 (Jan.) 1943

Skull Fractures and Brain Injuries. H. E. Mock, Chicago.—p. 1.
Wartime Industrial Surgery. N. K. Forster, Hammond.—p. 11.
Emergency Medical Service of Civilian Defense. W. S. Keller, Cleveland.—p. 16.
Medicine and Pharmacy—Shoulder to Shoulder. S. Badanish, Gary. —p. 22.
Ocular Manifestations of Multiple Sclerosis. B. J. Larkin, Indianapolis. —p. 26.

Journal of Experimental Medicine, New York

77:1-96 (Jan.) 1943

Studies on Hypoalbuminemia Produced by Protein Deficient Diets: III. Correction of Hypoalbuminemia in Dogs by Means of Large Plasma Transfusions. R. Elman and Harriet Wolf Davey, St. Louis.—p. 1.
Synergistic Action of Hemophilus Influenzae Suis and Swine Influenza Virus on Chick Embryo. F. B. Bang, Princeton, N. J.—p. 7.
Occurrence of Mucoid Polysaccharide in Hemolytic Streptococci of Human Origin. C. V. Seastone, Madison, Wis.—p. 21.
Quantitative Studies of Sulfonamide Resistance. W. M. M. Kirby and L. A. Rantz, San Francisco.—p. 29.
Virus of Infectious Feline Agranulocytosis: I. Characters of the Virus: Pathogenicity. J. T. Syverton, J. S. Lawrence, R. J. Ackart, W. S. Adams, D. M. Ervin, A. L. Haskins Jr., R. H. Saunders Jr., M. B. Stringfellow and R. M. Wetrich, Rochester, N. Y.—p. 41.
Id.: II. Immunologic Relation to Other Viruses. J. S. Lawrence, J. T. Syverton, R. J. Ackart, W. S. Adams, D. M. Ervin, A. L. Haskins Jr., R. H. Saunders Jr., M. B. Stringfellow and R. M. Wetrich, Rochester, N. Y.—p. 57.
Studies Concerning Site of Renin Formation in Kidney: IV. Renin Content of Mammalian Kidney Following Specific Necrosis of Proximal Convoluted Tubular Epithelium. M. Friedman and A. Kaplan, San Francisco.—p. 65.
Epidemic Keratoconjunctivitis: I. Isolation and Identification of Filtrable Virus. M. Sanders and R. C. Alexander, New York.—p. 71.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Radiology, London

16:1-30 (Jan.) 1943

Effects of Radiation on Workers. R. Peterson.—p. 3.
Accepted Standards in Radiologic Protection. S. Russ.—p. 6.
Radiologic Exploration of Sinus Tracts, Fistulas and Infected Cavities. H. C. Gage and E. R. Williams.—p. 8.
Method of Treatment for Carcinoma of Breast Including the Forequarter. C. W. S. Jerram and W. A. Langmead.—p. 26.
Note on Amebic Hepatitis. J. A. Ross.—p. 30.

British Medical Journal, London

2:745-774 (Dec. 26) 1942

Science of Health. J. A. Ryle.—p. 745.
Treatment of Superficial Tuberculous Lesions by Local Application of Promin. W. H. Tytler and A. D. Lapp.—p. 748.
Tuberculosis Deaths and the War. P. Stocks.—p. 750.
Artificial Respiration at Sea. G. H. Gibbens.—p. 751.
*Communal Feeding: Preliminary Report. E. B. Gunson.—p. 753.

Communal Feeding.—The communal feeding of some 10,000 Royal Ordnance Factory workers (mostly girls) resident at hostels adjacent to the factories, according to Gunson, seems to improve notably the health of these residents. This improvement can be attributed in part at least to the manner and method of the feeding arrangements. In general the types of food necessary for health are well appreciated, and these are supplied to the limit to which they are procurable. The catering management is in good hands, but more precise direction in the preparation of some particular foodstuffs is desirable and would be welcomed. The communal meal is a practical and economic arrangement so far as Royal Ordnance Factory workers living in hostels are concerned.

Edinburgh Medical Journal

50:1-64 (Jan.) 1943

*Outbreak of Diphtheria—Northern Palestine, 1940-1941. J. D. S. Cameron.—p. 1.
Acute Puerperal Breast Abscess: Clinical Observations on Its Etiology and Suggested Method of Treatment. A. I. S. Macpherson. —p. 25.
Medicine and History. D. Guthrie.—p. 31.
Studies on Stored Blood: XI. Phagocytosis in Stored Citrated Blood and Opsonic Power of Stored Liquid Plasma. J. W. Czekalowski. —p. 40.

Diphtheria in Northern Palestine.—An outbreak of diphtheria mainly confined to certain units, with one unit showing a heavy infection but with cases being widespread throughout all troop units in the area, is reported by Cameron. In the last war swabbing of contacts and isolation of carriers were sufficient to control most outbreaks. The outbreak occurred in the same theater of war as in 1914-1918. The frequent occurrence of acute cutaneous and nasal diphtheria alongside the faucial type was a further point demanding consideration. All suspected patients were hospitalized, and nasal and faucial swabbing was enlisted in the search for carriers. In investigating the native population it was found that Jewish children (who at the time had crusted and discharging noses) are the usual sufferers from diphtheria and that the British troops were brought into closer association with the Jews than with the Arabs. The most probable origin would appear to be the children of the country. In both children and troops the nose was the commonest source of the organism. Preventive measures in the army must be directed toward immunization of troops. The clearance of carriers among the civil population is a local government problem. After six months of continuous cases of diphtheria the outbreak was successfully ended by immunizing all personnel of the unit. Since then, ten months, no further cases have been reported although the unit has continued to stay in the area in which the infection was presumed to have arisen. In contrast, in another unit for which immunization was not instituted sporadic cases have continued. The same observation applies to several other units similarly treated. Isolation and swabbing alone appear not to answer the problem completely—a further justification for immunization of all personnel.

Book Notices

The 1942 Year Book of Industrial and Orthopedic Surgery. Edited by Charles F. Painter, M.D., Orthopedic Surgeon to the Massachusetts Women's Hospital and Beth Israel Hospital, Boston. Cloth. Price, $3. Pp. 424, with 302 illustrations. Chicago: Year Book Publishers, Incorporated, 1942.

This is the third review of this series, which is rapidly proving its worth. The compiler is well qualified for the task of selecting articles, authors and subjects. He has mature judgment. The subjects chosen are representative and well balanced. The authors are well recognized in their special fields. The general trend of the papers reviewed is toward traumatic, industrial, medicolegal and military subjects. The abstracts are well done, separating the wheat from the chaff and preserving the meat of the articles. The illustrations are reproduced satisfactorily. In this small volume one can obtain a bird's eye view of the progress and trend of orthopedic and traumatic surgery. The military application is emphasized. The intervertebral disk syndrome is discussed briefly. Some of the principal subjects covered are low back pain, the disk syndrome, arthritis, the Kenny treatment for infantile paralysis, the sulfonamides in orthopedic practice, osteomyelitis, burns, the scalenus syndrome, fractures of the hip, patella, humerus and elbow, wounds, amputations, soft tissue tumors, and tuberculosis of bones and joints. Operative procedures are described as well as advances in diagnosis. On the whole, the book is of the type eagerly awaited by the busy practitioner, who in this instance will not be disappointed.

Human Embryology. By Joseph Krafka Jr., M.D., Ph.D., Professor of Microscopic Anatomy, University of Georgia School of Medicine, Augusta. Medical Students Series. Cloth. Price, $4.75. Pp. 395, with 222 illustrations. New York & London: Paul B. Hoeber, Inc., 1942.

There is a widespread feeling in this country that the major ill of the medical curriculum is the failure of medical teachers to separate the important from the less important. In all the medical sciences—and arts—the rate of increase of new knowledge is ever increasing. This, with the addition of new sciences to the medical family, has made our present curriculum a monstrosity in which the student, armed with an array of encyclopedic textbooks, is required to learn much of the premedical and preclinical sciences and to spend an increasing period in postgraduate instruction. To remedy this condition various solutions are being considered by many of our leading medical schools. One of the results of this soul searching on the part of medical teachers is the appearance of a few smaller textbooks designed for students. Most, but not all, teachers feel that there is a great need for such textbooks but do not want quiz compends. The preparation of abbreviated books is difficult. The author or authors must possess a comprehensive knowledge of the field, including its controversies on unsettled questions. Perhaps the greatest danger in producing the shorter textbooks is the tendency to insert a short dogmatic sentence to cover a broad controversial subject.

With regard to this book, one cannot agree that an adequate consideration of experimental embryology is unnecessary. The discussion of heredity is much too brief for medical students. Some of the data usually presented in the laboratory work in embryology courses should be given in the textbook. The treatment of lymphatics is especially deficient. The illustrations could be improved; some are completely unacceptable.

A typical shortcoming of the book is shown in the following example of the insufficiency of a too brief—or unskilful—presentation. The student who wants to know is not helped by statements such as this on page 12 at the end of the chapter on historical development: "The last fifty years have seen the gradual development of an interaction theory, based on (1) definite localization of genes on the chromosomes (Morgan, 1910), (2) the modification of the action of genes by specific extrinsic factors such as chemicals (Stockard, 1909), temperature (Krafka, 1920), x-ray (Job, 1935), endocrines (Young, 1937), 'organizers' (Spemann, 1938), effective at 'critical moments' in development." If the purpose of providing smaller textbooks is to conserve the student's time, he is not being helped by a discussion which consists essentially of references to the original literature. The function of the author is to abstract the literature for the student, to present the most important questions, controversies and conclusions and to give or withhold references to the original literature according to his pedagogic inclinations.

The strongest feature of the book as contrasted with its many deficiencies is its insistence on human material, with reliance on that of the primates where the former is lacking. The recently obtained early human "ova" of Hertig and Rock make unnecessary much of the comparative data usually given. (Incidentally, why is a fertilized egg an ovum?) One may sympathize with the aims but be disappointed over achievements of this book.

A Text-Book of Fractures and Dislocations Covering Their Pathology, Diagnosis and Treatment. By Kellogg Speed, S.B., M.D., F.A.C.S., Professor of Surgery (Rush) of the University of Illinois, Chicago. Fourth edition. Cloth. Price, $12.50. Pp. 1,106, with 1,140 illustrations. Philadelphia: Lea & Febiger, 1942.

In this edition Speed presents the subject from the point of view of the principles involved and discusses treatment, as he states in his preface, on the basis of experience. To those seeking a quick reference work for a standard method of treating a fracture, the book may be somewhat disappointing. To students and practitioners, however, who want an understanding of the principles underlying the care of fractures it is highly satisfactory. The anatomic and physiologic facts relating to injuries in each region are briefly and clearly presented. Reproductions of roentgenograms, line drawings and photographs are used throughout the text and, with their terse descriptive titles, add much to the book. Each chapter is followed by a bibliography. The index of subjects which follows the text is complete. The first chapter, which deals with emergency handling of fractures, general methods of reduction, roentgenology, anesthesia and the technic of splinting, contains many valuable practical points. The second chapter, on the general outline of treatment of fractures, discusses minor and major procedures used, as well as indications for and against open operations. In the discussion of individual fractures throughout the rest of the book, these points of treatment are elaborated. It is evident throughout that the author is not in favor of the present tendency to standardize the technic for each fracture but insists on adapting the treatment to the particular circumstances. Consequently he discusses principles at length and outlines several technics which have been tried and found useful. His emphasis on the common complications and difficulties in handling various fractures adds greatly to the value of the book. The volume is long for any one looking for quick and easy information on the treatment of fractures. For those, however, who want an adequate discussion of the principles of fracture treatment this book is one of the best references for students and practitioners.

Divertículos idiopáticos del duodeno. Por Manuel S. Guitarte. Tesis de doctorado, Universidad nacional de Buenos Aires, Facultad de ciencias médicas, Escuela de medicina. Paper. Pp. 110, with 65 illustrations. Buenos Aires: Sebastián de Amorrortu e Hijos; "El Ateneo," 1941.

The concept of intestinal diverticula purely as a postmortem finding belongs to the past. Although no sign can be considered as pathognomonic, a careful analysis of the symptoms may anticipate in many cases what the radiologic examination will show more conclusively. This is the idea that the author develops in his thesis on the basis of the experience gained from a careful study of several patients. The prognosis and treatment of the condition are also considered, and the literature (two hundred and eighty-one references) is carefully reviewed.

Contribución al estudio de la epilepsia experimental en el hombre. Por el Dr. Isaac Roimiser. Tesis de doctorado, Universidad nacional de Buenos Aires, Facultad de ciencias médicas. Paper. Pp. 132, with illustrations. Buenos Aires, 1942.

Epileptic attacks of 38 patients as induced by pentamethylene were studied. This and analogous drugs have made possible an objective and controllable study of epilepsy comparable in every way to the spontaneous disease. Although the chief purpose of the author was the experimental study of the condition—and he does it quite thoroughly—the beneficial therapeutic effects observed are also recorded. The thesis is really a good monograph on the disease which the specialist would enjoy reading.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

TRANSMISSION OF FILARIA

To the Editor:—An article by Dr. Earl S. Taylor (The Journal, Dec. 20, 1941, p. 2123) states that "syphilis, malaria, influenza, measles, allergy, smallpox and diseases caused by the rickettsia organisms and, in the Orient, parasitic diseases such as filaria have been reported as transmitted by transfusion of whole blood." As far as I know, microfilariae must be sucked up by a mosquito in whose body they undergo a definite biologic cycle. When the cycle is completed they get into the proboscis and, when the mosquito bites, they break through the labium and actively penetrate the skin, presumably at the point of puncture by the mosquito. Filaria worms, for example Wuchereria bancrofti, do not live in the blood but in lymph spaces. Microfilariae are liberated into the blood, but when they are in the blood they are not infective, as they are just embryos which can further develop only in the mosquito. Would you be kind enough to tell me whether or not Dr. Taylor was right in his assumption that filarial diseases may be transmitted by the transfusion of whole blood and, if so, whether any such cases have been reported?

Rudolf W. Kogan, Minneapolis.

ANSWER.—Filaria infections cannot be transmitted directly by the transfusion of whole blood. The embryos (microfilariae) which circulate in peripheral blood need to be picked up by a susceptible blood sucking fly in its blood meal, after which they migrate from the fly's stomach to its thoracic muscles, where they metamorphose through a series of larval stages and migrate down the fly's proboscis sheath to enter the skin the next time the fly bites a human being. It is true, however, that microfilariae may be transferred from an infected individual to a filaria free person and may survive up to six weeks or more.

SENSITIVITY TO COCAINE AND IODINE BEFORE BRONCHOGRAPHY

To the Editor:—A recent issue of the *Lancet* or the *British Medical Journal* contained a statement that before one performs transcricothyroid bronchography patients should be tested for sensitization to iodine and cocaine. Can you give me a description of standard or generally employed tests for this purpose?

M.D., Iowa.

ANSWER.—Search of the literature reveals little information regarding tests for sensitivity to cocaine and iodine. As regards cocaine or cocaine substitutes, caution is strongly advised. Emil Mayer (THE JOURNAL, March 15, 1924, p. 876), heading a committee which investigated the toxic effects of local anesthetics, reported forty-six deaths, of which twenty-six were due to cocaine alone or with procaine. Some of these patients also received epinephrine to reduce local bleeding, but Mayer believes that the addition of epinephrine in amounts of 1 mg. or more to a solution of cocaine often increases the toxicity of the cocaine. He suggests that it is unsafe to inject more than 10 minims of a 1:10,000 dilution of epinephrine when used with cocaine or more than 1 mg. with procaine. Mayer also advises that in operative procedures in the larynx or bronchi cocaine be used in 10 per cent dilution, with two applications, totaling not over 15 minims, containing from 1 to 1½ grains (0.06 to 0.1 Gm.). Procaine should not be stronger than 1 per cent.

Louis Pelner, in a recent report on allergy to iodine (*J. Lab. & Clin. Med.* **27**:1150 [June] 1942), found that all 5 of his patients gave positive patch tests to iodine. He merely applied a drop of tincture of iodine to the skin. Within twenty-four hours all the sensitive individuals developed definite redness and swelling at the point of application. Nonsensitive persons were also tested but gave negative reactions. Pelner says "If this can be shown to be a general finding in other cases it can be used as a diagnostic test." The test is simple and should be tried before iodides are used or tincture of iodine is applied. In Pelner's series redness and swelling of the eyes and face and a fine scarlatiniform rash occurred in each case. In one case symptoms occurred after a saline laxative was taken which contained a small amount of iodine; in another the cause was a throat lozenge containing calcium iodide. A third patient developed symptoms from an iodoform pack, and the other two were affected by painting with tincture of iodine (1 of these developed thrombopenic purpura).

BUBBLE BATH PREPARATIONS

To the Editor:—A white girl aged 3½ years gives a history of rash. For the past year she has been using Bubble Foam and Feathertoam in her bath and I am interested in finding out what ingredients these articles contain. A paste patch did not show local reaction, but a symptomatic reaction was noticed on the following day.

John P. Helmick, M.D., Fairmont, W. Va.

ANSWER.—The ingredients of bubble bath preparations are salts which produce carbon dioxide when they are dissolved in water. Irritation following such a bath is ordinarily due to the carbon dioxide, a fine erythema sharply limited above at the high water mark. This lasts but a short time and is accompanied by a tingling sensation. Directions given for management of the carbon dioxide bath for therapy specify that the patient should be dried by patting, not rubbing. No report has been found of a persistent dermatitis caused by the carbon dioxide bath.

Another possibility is sensitization to the essential oils used to perfume the bath powder. Patch tests should be made to correspond as closely as possible with the conditions of the bath, the solution of salts diluted as in the bath and the carbon dioxide allowed to pass off before the patch is applied. A negative patch test, however, would not prove that the material tested was wholly innocuous.

OPERATIONS ON INFERIOR OBLIQUE MUSCLE

To the Editor:—At the present time three operations are mentioned for correction for an overacting inferior oblique muscle. It seems that tenotomy is no longer in vogue. However, myomectomy of the muscles or recession of the muscles has to be championed. Will you kindly advise me as to whether the more difficult recession has any actual advantage over myomectomy?

M.D., Michigan.

ANSWER.—No operator is justified in limiting his surgical armamentarium to any one operation on a given tissue. An overaction of an oblique muscle requires a different surgical attack than does an underaction. In the same way an advancement of an oblique muscle must be varied according to the amount and character of the correction desired. Consequently myectomy, recession and advancement all have their place, and the competent ophthalmic surgeon must be familiar not only with the technic but even more with the indications of each. A short but reasonably adequate discussion of this subject is to be found in the second edition of "Principles and Practice of Ophthalmic Surgery" by E. B. Spaeth (Philadelphia, Lea & Febiger, 1941, p. 191).

"STARCH EATING" AND NUTRITIONAL DEFICIENCY

To the Editor:—A colored woman has informed me that she eats large quantities of common gloss starch such as is used in washing clothes. She tells me that a great many people of her race in this locality eat as much as 2 cups a day. She appears to be in good general health. Is there any harm in this practice?

M.D., Ohio.

ANSWER.—"Starch eating" is a common dietary idiosyncrasy in certain localities and may lead to the development of deficiency diseases, particularly of vitamins of the B complex. Since starch supplies carbohydrate calories and is devoid of vitamins, protein and minerals, deficiency diseases may develop when calories derived from starch replace calories derived from foods of high vitamin content. If the person merely adds the starch to a diet of optimal vitamin, protein and mineral content, probably no harm would be done.

HYPNOTISM

To the Editor:—In The Journal, Jan. 23, 1943, page 299, M.D., Puerto Rico, is answered regarding the current status of hypnotism as a therapeutic procedure. On the whole the reply is fairly satisfactory, but I object to referring to such a book as "The Science of Hypnotism" by Alexander Cannon, New York, E. P. Dutton & Co., 1937. Immediately on reading the reply I opened my copy of Cannon's book, by chance, at page 87. It reads: "In disease the discomfort is produced by a deficiency in certain vibrations, including visual and auditory vibrations, and this means that the tuning-fork of the body, the etheric-double (which holds the astral to the physical body and should not be mistaken for the etheric body, which is still finer than the astral body) is 'out of tune' and needs adjustment. The correct colour is found which is required for the replenishing of the deficiency of the spectrum, and the correct sound should also be dealt with, by the use of gramophone records, choosing the right type of music which corrects the deflected auditory vibrations. The etheric vibrations of the higher realms are still unaffected and can be adjusted by hypnosis or such state induced by colour vibrations alone, auditory vibrations alone, or better still, the two combined. Perfumes, all of which are smell vibrations, also affect the human vibrations for good or evil. This can be observed in daily life. The constant smell of animals has often cured certain forms of insanity. I have used the Irwin colour filters for producing sedative, recuperative and stimulative influences upon the mind of man. The Deighton-Patmore psychic light (which consists of a red lamp surrounded by an orange bowl) brings out latent mediumship and hypnophilia." Unfortunately, such is the type of reference in one instance suggested to some one seeking reliable information. I hope you will correct this.

Milton H. Erickson, M.D., Eloise, Mich.